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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460
OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

EPA's Preliminary Supplemental Consideration of Certain Issues in Support of its Interim Registration Review Decision for Paraquat
January 30, 2024

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I. INTRODUCTION

In July 2021, the Environmental Protection Agency (EPA or the Agency) completed the *Paraquat Dichloride Interim Registration Review Decision* (Paraquat ID), which can be found in docket EPA-HQ-OPP-2011-0855 at www.regulations.gov. Paraquat dichloride (paraquat) is a restricted-use quaternary ammonium herbicide employed for weed control and as a harvest aid in the United States. The Paraquat ID finalized certain portions of EPA's analysis of paraquat's risks and benefits. The Paraquat ID also determined that certain mitigation measures were necessary for paraquat to meet the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) standard for registration.

In September 2021, the California Rural Legal Assistance Foundation, Farmworker Association of Florida, Inc., The Michael J. Fox Foundation for Parkinson's Research, Farmworker Justice, Alianza Nacional de Campesinas, Pesticide Action Network North America, Center for Biological Diversity, and Toxic Free North Carolina (Petitioners) filed a Petition for Review of the Paraquat ID in the U.S. Court of Appeals for the Ninth Circuit and subsequently filed a brief articulating various challenges to different aspects of the Paraquat ID, including concerns related to human health and EPA's balancing of risks and benefits. *See California Rural Legal Assistance Found'n, et al. v. USEPA*, Case No. 21-71287 (9th Cir.) In September 2022, the Court granted the EPA's unopposed motion to hold the case in abeyance to allow the Agency to further consider substantive issues raised by the Petitioners in relation to the Paraquat ID. In its declaration supporting the motion, EPA stated its intention to publish documents summarizing EPA's further consideration of those issues by January 2024 for public comment and then after taking significant public comment into consideration, finalize a document (or multiple documents) regarding those issues by January 17, 2025. Also, EPA noted its intention to present next steps at that time, if additional mitigation was determined to be appropriate.

This document presents EPA's preliminary consideration of the issues raised by Petitioners in relation to the Paraquat ID and the record supporting that ID, including concerns raised about the Agency's assessment of whether paraquat poses a risk of Parkinson's Disease, its analysis of respiratory and dermal exposures, as well as exposures to direct and indirect paraquat drift; the analysis of benefits; the consideration of health-related costs; and the required balancing of paraquat's risks and benefits. This document relies primarily on the record developed in support of the Paraquat ID, as the issues raised by Petitioners focused on the conclusions in the Paraquat ID issued in July 2021, with a couple of updates to correct discrepancies we have identified as part of this consideration. Comments on this document may be submitted to docket EPA-HQ-OPP-2011-0855 at www.regulations.gov.

While this document is based primarily on the existing record for the Paraquat ID, EPA notes that additional information has been submitted during the development of this document. That information has not been incorporated into this document due to timing constraints, but EPA intends to consider it as part of the next steps in this process. First, EPA recognizes that the Michael J. Fox Foundation and Earthjustice submitted letters to EPA on August 4, 2023, along with information that they believe is relevant to EPA's consideration of paraquat's health risks. This information consisted of approximately 90 submissions including scientific studies, as well as testimony filed in an ongoing state lawsuit concerning paraquat. EPA has included these

documents in the docket for paraquat at EPA-HQ-OPP-2011-0855-0317 and EPA-HQ-OPP-2011-0855-0313. While the Agency has started reviewing that material, it was unable to complete that review prior to the issuance of this document. [As a result, this document does not reflect the Agency's review of any of those materials.] Second, new information on paraquat vapor pressure was submitted on January 18, 2024, which may impact the Agency's volatilization analysis. Due to the late submission of that data, EPA has not incorporated that information into this document. Therefore, EPA intends to address that material along with any other significant information it receives during the public comment period and incorporate its consideration of those materials into any final document(s) issued by January 17, 2025.

II. SUMMARY OF EPA'S FURTHER CONSIDERATION OF CERTAIN ISSUES RELATING TO THE PARAQUAT ID

In the Paraquat ID, the Agency considered the risks and benefits of paraquat, along with any potential mitigation measures that could reasonably be applied to address the risks associated with the use of paraquat, consistent with the FIFRA mandate to ensure that registered pesticides do not pose "unreasonable adverse effects on the environment." The Agency prepared several documents to support its 2021 interim registration review decision for paraquat and attempted 'to connect the dots' of the risk-benefit information contained in its support documents in the Paraquat ID.

The present document draws on Agency documents available in the *Paraquat Dichloride Registration Review* docket, including available toxicological data considered sufficient to support risk management decisions to provide greater clarity about the Agency's reasoning and how it made its determination that paraquat would continue to meet the FIFRA standard for registration. This document provides greater clarity on the methodologies of the Office of Pesticide Programs (OPP), along with greater explanation of why those methodologies are protective, appropriate, and in accordance with its FIFRA mandate. This document also addresses the specific issues raised by the Petitioners in conjunction with the litigation concerning the Paraquat ID in Section V.

III. OPP'S REGISTRATION REVIEW PROCESS UNDER FIFRA

Before EPA may register a pesticide under FIFRA, a pesticide applicant must show, among other things, that the pesticide "will not generally cause unreasonable adverse effects on the environment." 7 U.S.C. 136a(c)(5); *see also* § 136a(c)(7). FIFRA section 2(bb) defines "unreasonable adverse effects on the environment," in part, to be "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide." 7 U.S.C. 136(bb)(1).[1] FIFRA also requires EPA to reevaluate every pesticide on a 15-year cycle to determine that each registered pesticide continues to meet the standard for registration 7 U.S.C. 136a(g); 40 C.F.R. 155.40. Given that science is constantly evolving and new scientific information can come to light at any time

[1] Although there are registered food uses for paraquat, EPA determined that aggregate exposures (including dietary exposures from food and drinking water as well as from residential exposures) were safe; therefore, FIFRA section 2(bb)(2) is satisfied. *See* 7 U.S.C. 136(bb)(2). For the remaining exposure scenarios, including occupational exposures, EPA evaluated risks and benefits under FIFRA section 2(bb)(1). *See id*. at § 136(bb)(1).

changing the understanding of potential effects from pesticides, these periodic reviews are important for reevaluating the effect of a pesticide on human health and the environment and ensuring that the pesticide still meets the FIFRA standard for registration.

While each pesticide review is unique, all pesticides go through the same basic registration review process outlined in EPA's regulations. 40 C.F.R. part 155, subpart C. The Agency initiates registration review by establishing a public docket for a pesticide registration review case and includes a Preliminary Work Plan summarizing information EPA has on the pesticide, the need for more data, and the anticipated path forward. The docket and workplan are available for a public comment period during which anyone may submit data or information for consideration by the Agency. The Agency considers information received during the comment period and develops a Final Work Plan, which includes facts about the pesticide and its current use and usage, anticipated risk assessment and data needs, and an estimated timeline for the review. 40 C.F.R. 155.50.

Within EPA, several divisions in OPP work together to evaluate and determine whether a pesticide meets the FIFRA standard for registration. The Health Effects Division (HED) assesses potential risks to human health from use of the pesticide, and the Environmental Fate and Effects Division (EFED) assesses potential risks to the environment from use of the pesticide. The Biological and Economic Analysis Division (BEAD) assesses economic, social, and environmental benefits of the use of a pesticide. The Agency will generally make the draft risk assessments and benefits analysis available for public comment. *See* 40 C.F.R. 155.53. In the case of registration review decisions, the Pesticide Re-Evaluation Division (PRD) weighs the assessed benefits of the use of the pesticide against the assessed costs (i.e., risks to human health and the environment from use of a pesticide and social costs, if any) and makes a regulatory determination about whether the continued registration of a pesticide poses "unreasonable adverse effects to the environment." 7 U.S.C. 136(bb).

EPA communicates its proposed findings and risk mitigation measures, among other things, in a proposed registration review decision or a proposed interim registration review decision and provides an opportunity for public comment. 40 C.F.R. 155.58. After considering any comments, EPA may issue either an interim or final registration review decision. 155.56, 155.58. Typically, registrants are expected to submit requests for amendment of registration(s), including any specified label changes, within 60 days after publication of the ID or final registration review decision. EPA published the Paraquat ID in docket EPA-HQ-OPP-2011-0855 and it is available at www.regulations.gov.

The "unreasonable adverse effects" standard under FIFRA section 2(bb)(1) imposes a risk-benefit balancing test on the Agency when evaluating pesticides for registration or in registration review.[2] As directed by FIFRA, determining whether there are unreasonable risks requires the

[2] In contrast, the Federal Food, Drug, and Cosmetic Act (FFDCA) requires that EPA conduct a risk-only analysis before establishing a regulation allowing for pesticide residues in or on food. The FFDCA standard, that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue," requires that the Agency's determination be based strictly on ensuring an absence of harm, unlike FIFRA, which allows risk that is not unreasonable and expressly requires consideration of benefits. 21 U.S.C. 346a(b)(2); *cf*. 7 U.S.C. 136(bb).

Agency to take into account the economic, social, and environmental costs and benefits associated with the use of the pesticide. As part of this balancing test, OPP considers, on the one side, the economic, social, and environmental "costs" of the use of the pesticide in terms of the risk imposed by use of the pesticide on human health or the environment. These could include, but are not limited to, health effects on the user through residential or occupational exposure; health effects on others such as farmworkers and bystanders or consumers of treated products; and effects on non-target organisms or the environment. On the other side of the equation, EPA considers the benefit of the use. Depending on the chemistry, benefits may include, for example, yield and/or quality losses avoided, abundant food supply, public health if managing a public health pest or management of animal pest-borne diseases, and managing an invasive species or nuisance pests in the home. For agricultural pesticides, the grower typically accrues the primary benefit from the use of the pesticide, as the pesticide is intended to reduce pest pressures on particular crops.

While FIFRA requires a determination of whether a pesticide presents an "unreasonable risk" and requires that determination to "tak[e] into account the economic, social, and environmental costs and benefits of the use of any pesticide," the statute provides discretion to figure out how to describe, calculate, and weigh those factors. Consistent with other EPA and federal government guidance, OPP does not view this balancing test to require a strict comparison of dollars on both sides of the risk-benefit equation. EPA guidance advises that "if important costs or benefits categories cannot be expressed quantitatively, they should be discussed qualitatively."[3] The Office of Management and Budget's Circular A-4, which defines good regulatory analysis and standardizes the way benefits and costs of Federal regulatory actions are measured and reported, advises that "if you are not able to quantify the [cost or benefit] effects, you should present any relevant quantitative information along with a description of the unquantified effects."[4]
In the assessment of pesticides, while EPA quantifies levels of risk to human health and ecosystems, those risk values do not readily translate directly into monetary values. Nevertheless, based on an understanding of the type and level of risk represented by those risk estimates, OPP is able to qualitatively weigh against benefits estimates to support the risk-benefit balancing analysis. Through this implementation of risk-benefit analysis, OPP implements the FIFRA section 2(bb) mandate by taking into account the "economic, social, and environmental costs and benefits of the use of any pesticide." For more detail, see the discussion of benefits balancing in Section IV.C.

[3] Environmental Protection Agency (EPA). 2010. Guidelines for preparing economic analyses. Accessed online on October 26, 2023 at: https://www.epa.gov/environmental-economics/guidelines-preparing-economic-analyses
[4] Office of Management and Budget (OMB). 2003. Executive Office of the President, OMB Circular A-4, Regulatory Analysis. https://www.whitehouse.gov/wp-content/uploads/legacy_drupal_files/omb/circulars/A4/a-4.pdf

A. Assessing the Human Health Risks of the Use of a Pesticide[5]

As a part of registration review, the Agency conducts a comprehensive screen of the entirety of the chemical's use profile and of available studies in its database. Through this process the Agency identifies any additional data needed to conduct the human health risk assessments as well as captures the updated understanding of the science and science policy that may impact the continued registration of products that contain an active ingredient. Under FIFRA, the Agency has the authority to require data submissions from the registrants of each pesticide product to fulfill the identified data needs. The Agency then conducts human health risk assessments with the available data to identify any potential risks of concern from the legal use of the pesticide.

As part of the risk assessment process, the Agency considers multiple sources of data to support registration review. The studies that are the most relevant and informative to risk assessment are those that clearly and fully describe the study design, conduct, and methods; report any underlying data that was obtained from the study; and include routes of exposure and doses relevant to risk assessment. These studies are often based on the Agency's data requirements in 40 C.F.R. part 158. Also, as part of registration review, the Agency conducts a broad survey of the available literature to identify studies relevant to human health risk assessment, particularly those that capture the aspects of the pesticide's toxicity beyond those accounted for in the Agency's toxicology database for that pesticide. Generally, this search strategy employs any terms restricted to the name of the pesticide, any common synonyms, and common mammalian models to capture as broad a list of publications as possible for that pesticide. When the science of a particular matter receives a great deal of public attention or where much research is available, the Agency may determine an additional focused assessment looking at a specific issue (e.g., the association between Parkinson's Disease (PD) and paraquat exposure) is necessary, in addition to the typical comprehensive risk assessment for registration review. When available, incident reports, which can include reports of any exposure or effect from a pesticide's use that was not expected or intended, are also referenced as a regular part of registration review as they can help determine if additional protection measures or clearer label instructions are needed.

The Agency's human health risk assessments estimate the nature, magnitude, and probability of harmful health effects in people who may be exposed to pesticides in the food and water they consume as well as through incidental ingestion, in the air they breathe and contact with the skin through their use of the pesticide at home and work, as a result of activities that may lead to contact with residues on treated surfaces, drift, and volatilization.

The Agency develops human health risk assessments for pesticides using the National Research Council's four-step process[6]:

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[5] Although EPA's FIFRA analysis also typically considers the environmental fate and potential risks to the environment from use of the pesticide, this document does not contain any discussion of those issues. The agreement for holding this case in abeyance focuses on issues related to non-dietary human health, benefits, and risk-benefit balancing, not environmental issues. Petitioners did not raise issues relating to EPA's assessment of environmental or ecological impacts.

[6] This process is described on EPA's website. *See* https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/assessing-human-health-risk-pesticides. *See also* Fowle III, JR and Dearfield, KL. (2000). US Environmental Protection Agency Risk Characterization Handbook. EPA 100-B-00-002. https://www.epa.gov/sites/default/files/2015-10/documents/osp_risk_characterization_handbook_2000.pdf.

- Step One: Hazard Identification (Toxicity)
- Step Two: Dose-Response Assessment
- Step Three: Exposure Assessment
- Step Four: Risk Characterization

To identify hazard (or the toxicity that might be posed by a pesticide) for the purposes of human health risk assessment, the Agency examines whether a pesticide has the potential to cause harm to humans, and if so, under what circumstances. In this step, the Agency considers the full spectrum of potential health effects that may occur from different types of pesticide exposure, from eye and skin irritation to cancer and birth defects. The Agency considers data submitted to the Agency under FIFRA (often animals studies conducted consistent with EPA's data requirements), as well as public literature and other supporting information. Whether a particular study or effect will be utilized for risk assessment purposes depends on many factors, including, but not limited to, route of exposure, dose-response relationship, and statistical and biological significance, among others. A comprehensive description of this evaluation process is provided further below in Section V.A.

Briefly, in conducting a dose-response assessment for human health risk assessment, the Agency examines the numerical relationship between pesticide exposure ("dose") and identified toxicological effects ("response") to establish points of departure (PODs) that would be relevant for human oral, dermal, and inhalation exposures based on the pesticide's use pattern. PODs are commonly derived from studies conducted with laboratory animals for which the Agency has established the lowest dose where harmful or adverse effects are observed in the test animals (i.e., the lowest observed adverse effect level (LOAEL)) and the highest dose at which no statistically or biologically significant adverse effect is seen (i.e., the no observed adverse effect level (NOAEL)).[7] Even if an adverse effect is identified, it may not be used in risk assessment if it occurs at an exposure level unlikely to be encountered by humans during everyday applications of a pesticide. For example, 1000 mg/kg/day is often considered the limit dose in animal studies and is not relevant for human health risk assessment.

After identifying NOAELs and/or LOAELs, the Agency determines the appropriate uncertainty or safety factors for use in assessing exposure as well as the uncertainties that are built into the dose-response assessment. Uncertainty factors (UFs) are typically employed to account for the uncertainty involved in extrapolating from animal data to humans (i.e., an interspecies uncertainty factor) and to account for the potential variation in sensitivity among humans (i.e., an intraspecies uncertainty factor), as well as other factors that may be employed to address other uncertainties in the database or gaps in available data. These UFs create an additional margin of safety for protecting people who may be exposed to pesticides. For more information on the UFs, please see Section V.A. A typical unrefined risk assessment uses the default UFs, which include a 10-fold safety factor for both intraspecies and interspecies effects for a total of 100x, although

[7] The approach described is the most typical approach used for identifying a POD, although OPP may employ alternative methodologies, depending on the circumstances. For example, if a NOAEL cannot be identified, EPA may use the LOAEL as the POD or use modeling to derive a benchmark dose. *See infra*, note 8; USEPA, "Benchmark Dose Technical Guidance" (June 2012), located at https://www.epa.gov/sites/default/files/2015-01/documents/benchmark_dose_guidance.pdf.

EPA may use different UFs where appropriate.[8] For uses that contribute to aggregate exposure analysis under the Federal, Food, Drug, and Cosmetic Act (FFDCA), EPA is required to retain an additional 10-fold safety factor, as necessary to protect infants and children, unless reliable data exists demonstrating that a different safety factor would be protective. 21 U.S.C. 346a(b)(2)(C). This additional factor (often referred to as the FQPA Safety Factor (SF), after the Food Quality Protection Act that enacted this provision) often overlaps with other UFs that account for the completeness of the overall database (e.g., lack of a NOAEL, extrapolation from subchronic to chronic, special susceptibility of infants and children).[9]

The Agency's exposure assessment examines frequency, timing, and amount of contact a person may have with a pesticide. Typical sources of pesticide exposure include dietary exposure (which includes food and drinking water), residential, bystander (e.g., spray drift), and occupational exposures. This part of the assessment is tied closely to the registered uses, in that EPA assesses exposure scenarios that are likely to result from the registered use patterns of the pesticide.

The final step of the process entails risk characterization. In this step the Agency summarizes and integrates the hazard, dose-response, and exposure assessments to synthesize an overall conclusion about risk for a pesticide. The assumptions and uncertainties built into the risk assessment are explained, and the strength of the database is considered, to help inform and draw conclusions about the nature and extent of the risk from exposure to the pesticide.

Simply put, the risk to human health from pesticide exposure depends on both the toxicity of the pesticide and the likelihood of people coming into contact with it:

Risk = Toxicity x Exposure.

In order for there to be a risk from the pesticide, there must be some toxicity and exposure; a lack of toxicity or exposure will not result in a finding of risk. For non-dietary human health effects,[10] EPA assesses whether a certain pesticide or use of a pesticide presents a potential non-dietary risk to humans by comparing the Margin of Exposure (MOE) to a Level of Concern (LOC).[11] MOEs represent the magnitude by which the POD (e.g., often the NOAEL of the critical toxic effect) exceeds the calculated dose of pesticide exposure for a given exposure scenario based on approved use patterns, where both are expressed in the same units. The LOC is a combination of the UFs (i.e., interspecies, intraspecies, FQPA SF or any additional uncertainty). When the MOE

[8] For example, OPP can use Physiologically-Based Pharmacokinetic (PBPK) modeling to refine uncertainty factors when assessing a pesticide's potential risk. *See* USEPA, Physiologically Based Pharmacokinetic Modeling to Address Pharmacokinetic Differences Between and Within Species (August 3, 2017).

[9] For a more detailed discussion of the Agency's dose-response assessment and application of uncertainty factors, see USEPA, Determination of the Appropriate FQPA Safety Factor(s) in Tolerance Reassessment (Feb. 28, 2002), at https://www.epa.gov/sites/default/files/2015-07/documents/determ.pdf.

[10] Because the Petitioners did not raise any issues with regard to dietary human health risks, EPA is focusing this response on its approach to non-dietary human health risks.

[11] *See* USEPA, General Principles for Performing Aggregate Exposure and Risk Assessments, at 51, located at https://www.epa.gov/sites/default/files/2015-07/documents/aggregate.pdf. *See also* the Agency's general approach to human health risk assessment described here: https://www.epa.gov/iris/reference-dose-rfd-description-and-use-health-risk-assessments

is less than the LOC, OPP considers the scenario to present a potential risk of concern because the estimated exposure exceeds the margin of safety imposed on the POD. By contrast, when the MOE is equal to or greater than the LOC, the presumption is that the scenario does not result in a potential risk of concern because expected exposure is less than the level needed to maintain the margin of safety applied to the POD.

Where the risk analysis indicates that there may be risks of concern from exposure to a particular pesticide, OPP may consider whether there are available data to refine the risk assessments.[12]

B. Assessing the Benefits of the Use of a Pesticide

BEAD is responsible for analyzing the benefits of the use of a particular pesticide, and this includes assessing the magnitude of the benefit(s) of a particular pesticide. Benefits maybe described qualitatively or measured quantitatively. Depending on the chemistry, benefits may include yield and/or quality losses avoided, abundant supply of food and fiber, public health if managing a public health pest or management of animal pest-borne diseases, managing an invasive species, to name a few. In many cases, including pesticides used in crop production, benefits may be based on various agronomic factors, chemical characteristics of a particular pesticide, and alternative control strategies, which influence how a user or grower manages pests. When possible and when appropriate, BEAD will describe the benefits in both monetary (e.g., dollars saved by not having to use alternative chemistries) and non-monetary (e.g., chemical characteristics that make it easy to use or an important tool in resistance management) terms as both can be important for informing a sound policy decision.

In the case of paraquat, a pesticide that primarily has agricultural applications, BEAD found the benefits primarily accrue to the grower. When appropriate, the Agency also considers other benefits that may result from the use of the pesticide (or costs from not using the pesticide). While it is a rare occurrence that one chemistry would have commodity or consumer price effects, BEAD did examine that issue but did not anticipate market level effects in the case of paraquat.[13,14]

EPA's guidelines for preparing economic analyses indicates that the "economic and other impacts of policies or regulations are measured as the differences between these two scenarios: a "baseline scenario," which describes "the world absent the proposed regulation or policy action" and a "policy scenario," which describes "the expected state of the world with the proposed policy or regulation in effect."[15]

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[12] See e.g., https://www.epa.gov/expobox/exposure-assessment-tools-tiers-and-types-screening-level-and-refined

[13] See section 'Regional and National Level Impacts' in English and Hodde, 2020. Paraquat Dichloride (PC# 061601) Use in Soybeans: Usage, Benefits, and Impacts of Potential Mitigation. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0212

[14] See section 'Market-Level Impacts of Not Using Paraquat' in Coy and Kells, 2020. Paraquat Use on Peanut: Usage, Benefits and Impacts of Potential Mitigation for Registration Review. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0211

[15] Environmental Protection Agency. 2010. Chapter 5 from Guidelines for preparing economic analyses. Available at: https://www.epa.gov/environmental-economics/guidelines-preparing-economic-analyses

During the registration review assessment of an agricultural pesticide,[16] the pesticide in consideration is registered so BEAD describes the baseline scenario to be an overview of how (e.g., application methods), when (e.g., timing over the course of a growing season), where (e.g., regions), and why (e.g., target pests) a pesticide is currently used, based on the product's current approved labeling. The baseline may also include a description of outcomes that a grower of a particular use site realizes, such as crop yield or income, when employing that pesticide. Generally, BEAD will assess multiple use sites and may distinguish multiple regions within the United States since pests and production practices may vary across the nation. The policy scenario then, is grower outcomes without the use of the pesticide. BEAD identifies likely ways a grower would manage the identified target pests in the absence of the pesticide and assesses the consequences (e.g., financial impacts from decreased yield or crop quality, or increased costs of alternative methods of pest control). The difference between the two scenarios conveys the importance of the subject pesticide to the grower, i.e., the magnitude of its benefit. For example, BEAD may find that a particular pesticide targets an economically damaging target pest for which few alternative pesticides are available. In its absence, a grower may realize yield losses, lower income due to reductions in crop quality, and/or increased pest control costs. BEAD may be able to measure these impacts against the income growers receive from producing a crop when using the pesticide. The benefits assessment may also include an assessment of the impacts of various mitigation measures, since as the cost of mitigation measures increase the net benefits of use of the pesticide may diminish.

Benefits assessments are often supported by information and efficacy data from university extension services, the U.S. Department of Agriculture (USDA) (e.g., publicly available crop production, pesticide usage, and cost data as well as information submitted directly to EPA), public and commercially available grower survey data, and public comments submitted to the Agency from various stakeholders.

C. Issuing a Registration Review Decision on a Pesticide

If there are no potential risks of concern identified through the risk assessments, then the Agency would generally determine that the pesticide poses no unreasonable risks and can continue to be registered without any changes to the legally registered uses. If potential risks of concern are identified, the Agency will work to ensure that those risks are not unreasonable. In some cases, additional mitigations may be available that are highly feasible, practical, and economical (e.g., gloves or other protective clothing) without having a significant impact on the benefit of the pesticide's use and fully mitigate the risk of concern. In that case, the Agency would choose to require appropriate mitigation and issue a decision. In instances where different mitigations options are available to mitigate the risk, the Agency will consider various options in conjunction with relevant use and usage patterns (e.g., what option mitigates the risk but is most feasible, practical and economical).

[16] EPA conducts the risk-benefit balancing analysis for all registered pesticides, which includes more types of pesticides than just those used in agriculture. EPA is writing this document in terms of the process for agricultural pesticides as it is most relevant to paraquat, which is used as an agricultural pesticide.

Table 1 below lists some examples of potential risk concerns that may be identified in a registration review human health risk assessment along with some examples of mitigation options that the Agency may consider to mitigate the risks that have been identified.

Table 1. Human Health Risks That Could Be Identified During Registration Review

Examples of Potential Human Health Risk of Concern Under FIFRA	Examples of Potential Options for Mitigation
Residential Handler	• Application rate reductions; • Limits to certain formulations; • Use cancellation.
Bystander	• Spray drift management (e.g., windspeed restrictions, changes to droplet size, boom heigh restrictions, buffers); • Use cancellation.
Occupational Handler (Mixer/Loader or Applicator)	• Personal Protective Equipment (PPE) (e.g., respirators, gloves); • Engineering controls (e.g., enclosed cabs, closed loading systems); • Rate reductions; • Application equipment restrictions; • Use cancellation.
Occupational Post-Application	• Restricted Entry Intervals (REI); • Use cancellation.

OPP's process of considering alternative mitigation options is essentially equivalent to the process of considering alternative regulatory or policy options as would be done in a typical cost-benefit analysis. OMB and EPA's National Center for Environmental Economics (NCEE) provide guidance on the process of considering various policy options when conducting a cost-benefit analysis.[17] In addition to weighing the risks and the benefits of a particular use for which potential risks of concern have been identified, the Agency often simultaneously considers the assumptions within the modeled scenario and whether those assumptions reasonably represent "widespread and commonly recognized practice," as required in FIFRA section 3(c)(5)(D), 7 U.S.C. 136a(c)(5)(D). The Agency will also consider the nature of the effect (risk) associated with the relevant pesticide exposure, e.g., whether the potential effect is likely to be acute or chronic. Taking all these factors into consideration, Agency risk managers may evaluate various policy approaches (e.g., imposing mitigation measures from minor PPE to cancellation, conducting potential refinements of the assessments) to determine if there is a regulatory approach that supports a determination that the continued registration will not pose unreasonable adverse effects on human health or the environment. This objective of identifying the most economically efficient approach is in line with EPA's NCEE's guidance for regulatory analyses.

The assessment of the impacts of mitigation options is often included with the assessment of benefits of the use of the chemical conducted by BEAD. For example, when considering if a respirator is likely to be an effective mitigation strategy to address an identified occupational

[17] Environmental Protection Agency (EPA). 2010. Chapter 5 from Guidelines for preparing economic analyses. Accessed online on October 26, 2023 at: https://www.epa.gov/environmental-economics/guidelines-preparing-economic-analyses

handler inhalation risk of concern, the Agency considers the impacts of imposing that mitigation option. In essence, the risk manager will weigh how much risk reduction may be achieved by a particular mitigation measure against how much impact imposing that mitigation measure will have on the net benefits of using the pesticide. Generally, OPP will seek to choose the least burdensome mitigation option that will result in exposures that do not result in risks of concern, i.e., the MOE is greater than the LOC, as a way to ensure that the risks of the pesticide are not unreasonable as directed by FIFRA.

Assessing the impacts of various mitigation measures includes a consideration of any cost burden (e.g., costs of purchasing and maintaining respirators, stress on the wearer) and how the mitigation may complicate a growers' pest management practices when compared to the current label requirements (e.g., no respirator). For example, in some instances, the Agency may consider imposing a respirator requirement to address mixer/loader inhalation risks. The Agency will weigh how much risk reduction may be accomplished through the respirator requirement (e.g., does it fully or partially mitigate the risk concern) against the impacts of that mitigation (e.g., the cost of initial respirator purchase, the cost of replacement filters, the associated requirement that all users of the respirator have an annual fit test, as well as the potential for heat stress that can result from use of a respirator and any potential burden that may result for more frequent breaks required to prevent heat stress.) If that respirator requirement fully mitigates the risk concern but the costs of that respirator requirement are so high that it is effectively equivalent to cancellation of the use (essentially, a loss of all benefits of use), the Agency may consider a different mitigation option and weigh the nature or extent of any remaining risk with that different mitigation measure with the net benefits under that other mitigation scenario.

Generally, if an agricultural pesticide is determined to provide high benefits, that means that its use is of great importance to a grower on a per acre basis (e.g., the pesticide is highly effective for an economically important pest, other chemistries are not available or as effective on one or more target pest, it was identified to be important for resistance management and/or cheaper than identified alternatives). Therefore, if the proposed measures to fully mitigate risk would significantly impact or reduce the benefit estimated from the use of the pesticide (i.e., essentially prohibiting the use of the pesticide), the Agency may consider whether a less stringent mitigation strategy could effectively reduce risks to the point where any remaining risks are outweighed by the high benefits of the pesticide. This strategy is consistent with the FIFRA standard to ensure that risks are not "unreasonable" while "taking into account the economic, social, and environmental costs and benefits of the use of any pesticide." As stated in the statute, the FIFRA standard does not require the Agency to ensure that all risks are fully mitigated, only that the risks not be unreasonable and that the pesticide does not cause "unreasonable adverse effects to man or the environment." 7 U.S.C. 136(bb).

For a case where EPA has determined there are low benefits, that is usually because there are alternative pesticides available with similar anticipated cost and effectiveness. In these cases, the imposition of mitigation measures may have relatively small impact on the pesticide user while reducing the risk, since the user can easily find an alternative.

When working to balance risk reductions and the associated impact on a pesticide user, the Agency also considers the uncertainties of alternative policy approaches (mitigation options).

The Agency will consider how refined model inputs or understanding of any identified uncertainty could inform or alter the Agency decision and risk/benefit outcomes. If greater insight into identified uncertainties would substantially change the decision, the Agency may seek stakeholder input either via targeted outreach or solicit public comments in its risk assessments or proposed decision.

If, after considering risks, benefits, and available mitigation options, EPA concludes that the pesticide will not cause "unreasonable adverse effects on the environment," the pesticide may remain registered, as long as the registrant takes all required action required in the final registration review decision. *See* 40 C.F.R. 155.40, 155.57, 155.58. However, if the Agency determines that the pesticide causes unreasonable adverse effects on the environment, the Agency may take action against the pesticide, including cancellation. *See* 40 C.F.R. 155.40; 7 U.S.C. 136d(b).

IV. RECENT REGISTRATION REVIEW OF PARAQUAT, FINDINGS, AND DECISION

A. Potential Human Health Risks of Paraquat

In the *Paraquat Dichloride: Draft Human Health Risk Assessment in Support of Registration Review* (HHRA), the Agency assessed risks to human health and did not identify dietary risks of concern from exposure to paraquat[18]. The Agency did not conduct residential handler and residential post-application assessments because there are no products registered for application to residential areas. The HHRA did identify potential risks of concern to bystanders, occupational handlers, and those conducting post-application activities; however, EPA identified risk mitigation measures that would fully mitigate risks for all scenarios (and without which the pesticide would not meet the standard for registration), except for those scenarios listed in Table 2 below. Registrants have adopted all of the mitigation measures identified in the Paraquat ID.

Although Parkinson's Disease (PD) is not an expected result of the pesticidal use of paraquat, a connection has been hypothesized throughout the scientific literature, and so out of an abundance of caution, the Agency conducted a systematic review to assess the relationship between paraquat exposure and PD. After a thorough review of the relevant studies, the Agency concluded that the weight of evidence was insufficient to link paraquat exposure from pesticidal use of U.S. registered paraquat products to PD in humans. The few studies from the open literature that report effects in animal models considered to be PD-like hallmarks from exposure routes anticipated for pesticidal uses (e.g., oral, dermal, inhalation) observed these effects following subchronic oral exposure to dose levels at least 14 times above the current subchronic PODs. Furthermore, the toxicity profile for paraquat indicates that contact toxicity and effects in the respiratory and renal system occur at lower doses than those eliciting neurotoxicity in animal

[18] "HHRA" is used in the remainder of this document to refer to both of the following documents: Britton, W. et al., 2019. Paraquat Dichloride: Draft Human Health Risk Assessment in Support of Registration Review. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0121 and, Britton, W., 2020. Paraquat Dichloride: Draft Human Health Risk Assessment in Support of Registration Review, Paraquat Dichloride: Addendum to the Memorandum, 'Draft Human Health Risk Assessment in Support of Registration Review' Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0215.

models. Consistent with EPA practice, the paraquat human health risk assessment evaluated risk based on the most sensitive endpoints identified through available data (i.e., skin irritation and upper respiratory tissue irritation (i.e., throat/vocal cords) in route-specific dermal and inhalation studies, respectively). Therefore, the selected PODs account for and are protective of (i.e., PODs are based on effects that are more sensitive and occur at a lower dose than) the limited evidence of neurotoxic effects reported in the open literature for routes of exposure relevant to the paraquat human health risk assessment.

The HHRA applied the full 10-fold safety factor for both intraspecies (UF_H = 10x) and interspecies (UF_A = 10x) variation to the studies that EPA determined to provide the most sensitive, human-relevant endpoint in the available information. This accounts for studies in animals used to determine health outcomes in humans and is meant to be protective of effects in the most sensitive individuals or population subgroups (e.g., age or ethnicity). The FQPA SF was reduced to 1x for all relevant scenarios because the Agency concluded that there was reliable data indicating that the 1x SF would be protective of effects in infants and children. The toxicity database, along with contributions from open literature, was deemed sufficient to adequately assess risk for infants and children. The PODs are considered protective of all known health effects resulting from paraquat exposure, including those identified in the toxicity database and any evidence of susceptibility or neurotoxicity captured in the open literature. Furthermore, the dietary and non-occupational (e.g., spray drift) assessments were conducted using conservative assumptions regarding exposure and will not underestimate exposure. Therefore, the resulting LOC (LOC= UF_H x UF_A x FQPA SF) for the paraquat assessment is 100.

Table 2 below highlights the scenarios identified during registration review for paraquat where the Agency found potential dermal (skin irritation) and inhalation (upper respiratory irritation) risks of concern to agricultural workers after accounting for the mitigation identified in the ID and adopted by registrants. The table also includes a column with the resulting risk estimates or MOEs considering the mitigation where applicable. As noted earlier, when the MOEs are below the Agency's calculated LOC, the scenario may present a potential risk of concern because the estimated exposure exceeds the margin of safety built around the dose at which no adverse effects were observed.

Table 2. Summary of human health risks following implementation of Paraquat ID mitigation (LOC for all scenarios in the table is 100)

Risk category	Mitigation Identified in the Paraquat ID to Reduce Relevant Risk	Potential Human Health Risks Remaining after Implementation of the Paraquat ID Mitigation
Potential inhalation risks to aerial applicators from aerial applications made for cotton desiccation	None	Inhalation risk based on portal of entry (upper respiratory irritation) POD. MOE = 71.[a]
Potential dermal risks to workers involved in cotton harvest (picker operator, raker, and tramper) due to post-application cotton desiccation scenarios	7-day restricted entry interval (REI)	Dermal risks based on skin irritation at 7-day REI. MOEs considering 7-day REI = 25-52.[b]
Potential inhalation risks for ground applicators making certain high acreage (more than 80 acres) applications using enclosed cabs [c]	Enclosed cabs for any individual making high acreage applications (more than 80 acres) in a 24-hour period	Inhalation risk based on portal of entry POD. MOEs considering enclosed cabs= 52-87.
Potential inhalation risks for ground applicators making certain low acreage (80 acres or less) applications using open cabs [d]	PF10 respirators or use of enclosed cab for any individual making applications of 80 acres or less within a 24-hour period	Inhalation risk based on portal of entry POD. MOEs considering PF10 respirator = 76-95. Enclosed cab fully mitigates the risk.

[a] See Appendix A. for additional clarification on the occupational inhalation risks MOEs for this scenario.

[b] See Appendix A. for additional clarification on the post application MOEs. MOEs for post-application cotton desiccation scenarios updated from those presented on page 35 of the ID where the application was considered at the 1.0 lb active ingredient (AI)/acre rate. At the 1.0 lb AI/acre rate, "harvesting, mechanical, and module builder operator" also resulted in risks of concern; however, a rate of 0.5 lb AI/acre or less is used for cotton desiccation (harvest aid). 'Harvesting, mechanical, module builder operator' is not a scenario of concern at a 7-day REI when considering the 0.5 lb AI/acre rate.

[c] Three scenarios result in potential risks of concern after considering the use of enclosed cabs including applications of 1 lb AI/acre to barley, coniferous/evergreen/softwood (non-food), corn, cotton, fallowland, peanuts, peas, rice, safflower, sorghum, soybean, sugarcane, sunflower, tyfon, wheat; 0.85 lb AI/acre to legume vegetables, mint; and 0.6 lb AI/acre to grasses grown for seed, and potato.

[d] Three scenarios result in potential risks of concern after considering the use of PF 10 respirators including applications of 1 lb AI/acre to artichokes, asparagus, brassica, vegetables, carrots, corn, cucurbit vegetables, eggplant, flower plants, fruiting vegetables, garlic, ginger, leafy vegetables, lettuce, manioc, melons, okra, onions, peas, pepper, pineapple, root and tuber vegetables, rhubarb, sugar beet, tomato, turnip greens, yam; 0.94 lb AI/acre to tobacco; and 0.80 lb AI/ acre to legume vegetables, sage, clary, taro, and other vegetables.

Description of the potential residual risk effects

EPA has identified two exposure scenarios for which potential risks remain after mitigation from the use of paraquat as a cotton harvest aid: (1) for applicators from aerial applications and (2) to workers engaged in post-application harvest activities including picker operator, raker, or tramper cotton harvest aid. In addition, EPA identified potential occupational handler risks of concern for individuals making groundboom applications to certain crops (see Table 2 above and Section IV.C. for a detailed discussion of the scenarios where potential risk concerns remain).

The potential inhalation risks of concern reflect the fact that the primary target organ of paraquat is the lungs. Evidence of lung inflammation, scarring, and compromised lung function in response to paraquat exposure are observed throughout the toxicity database in different species (rats, mice, and dogs). Effects in the respiratory tract are observed after single and repeat dose exposures regardless of the route of exposure (oral or inhalation); however, inhalation was a more sensitive route of exposure than the oral route in both acute and repeat dose studies. Because this was the most sensitive route of exposure, (i.e., the one that will cause the most significant health effect), protecting for this scenario also protects for any secondary effects. For further discussion of this point, see Section V.A. Paraquat is moderately to severely irritating to mucous membranes leading to portal of entry toxicity in the upper respiratory tract from repeated inhalation. The potential for inhalation risks of concern from aerial cotton desiccation applications and the ground application scenarios identified in Table 2 are based on this effect.

The potential risk of concern resulting from activities conducted after applications of paraquat are made for cotton desiccation are based on a dermal endpoint. Based on the toxicity database, the Agency has determined that paraquat causes minimal skin irritation in rabbits following acute dermal exposure and elicits a more varied and corrosive dermal response (scabbing, hyperkeratosis, epidermal erosion/ulceration, surface exudation, acanthosis, and inflammation) with prolonged, repeated exposure. This response is consistent with dermal toxicity as described in the human incident report. Skin damage was the most commonly reported symptom for human incidents resulting from occupational use and ranged from blisters and dry skin to chemical burns and lesions.

The inhalation and dermal points of departure described above are based on the most sensitive endpoints in EPA's database. Parkinson's Disease is not an expected health outcome of pesticidal use of paraquat, based on the Agency's analysis of the materials it has reviewed to date. For a more detailed discussion see Section V.A. below.

B. Benefits of Paraquat

Paraquat can be used as a contact, broad-spectrum herbicide to control unwanted broadleaf and grass weeds or to remove a cover crop, as a plant growth regulator to prepare a crop for harvest, and for sucker control on perennial crops.

Several chemical characteristics of paraquat can make it useful. It has a unique mode of action that makes paraquat beneficial as a resistance management tool. Paraquat is rapidly absorbed into plant tissues, which means that control of vegetation occurs, even at cool temperatures when

plants are not actively growing or when applied shortly before a rain event (i.e., rainfast). Generally, alternatives either require plants to be actively growing or are not as rainfast as paraquat.

BEAD assessed the benefits of the use of paraquat in various use sites. The findings were presented in four documents: an overview document covering multiple use sites, and three separate documents covering cotton, peanuts, and soybeans.[19,20,21,22] After receiving public comments on the proposed interim registration review decision (PID) and the BEAD documents that informed the PID, BEAD issued a Response to Comment memorandum.[23] Given paraquat's characteristics and considering other available weed control measures, BEAD determined that use of paraquat has high benefits for numerous crops and crop groups including artichoke, cotton, peanuts, soybeans, bulb vegetables, cucurbits, alfalfa, orchards, and vineyards. BEAD also found that the benefits of paraquat were low for various crops and non-crop groups including grains (e.g., corn, winter wheat, and sorghum), tomato, and pastureland. Due to limited information for some use sites, BEAD found that the benefits are uncertain for nursery production, rights of way, commercial/industrial buildings, and storage yards.

In the following paragraphs, benefits information is provided for the use sites analyzed in detail by BEAD.

Cotton

Paraquat is used as a preplant burndown herbicide in cotton and is a commonly used harvest aid in certain states including Texas, California and Arizona. As an herbicide, paraquat offers control of a wide range of emerged weeds, especially in cool conditions when plants are not actively growing. Paraquat is also an important part of managing herbicide-resistant weeds because it offers a unique mode of action. As a harvest aid, paraquat is fast acting and is used to make the leaves dry up and fall off the plant prior to harvest. Generally, these growers get the benefit of being able to harvest more quickly than they may be able to if using an alternative due to the fast-acting nature of paraquat. Timely harvest is important because the more time between application and harvest, the greater the likelihood of a rain event that can reduce the quality of the cotton fibers and lower the market value. Given this information, BEAD determined that use of paraquat has high benefits for cotton growers.

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[19] Harty, T., et al. 2020. Overview of Use, Benefits and Impacts of Mitigation Assessment for Paraquat (PC# 061601) in Agricultural Settings. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0210.

[20] Hanson, C., and Chen, C. 2020. Paraquat Dichloride (Herbicide and Harvest Aid) Use, Usage, Benefits and Impacts of Potential Mitigation in Cotton (PC# 061601). Available at https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0213

[21] Coy, M. and Kells, B. 2020. Paraquat Use on Peanut: Usage, Benefits and Impacts of Potential Mitigation for Registration Review. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0211

[22] English, L. and Hodde, W., 2020. Paraquat Dichloride (PC# 061601) Use in Soybeans: Usage, Benefits, and Impacts of Potential Mitigation. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0212

[23] English, L., et al. 2021. BEAD Response to Paraquat Usage and Benefit Related Comments Received on the Preliminary Interim Decision of Paraquat. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0308

If growers could not use paraquat as an herbicide, then growers would need to use an alternative herbicide (e.g., glyphosate, flumioxazin, glufosinate). In addition, these growers could face reduced control of key weeds targeted by paraquat, and possibly yield losses. Additionally, growers would lose a unique mode of action as a rotational partner for delaying herbicide resistance.

As a harvest aid in cotton, applications of paraquat are regionally important; it is primarily in the southwest region of the United States (Texas, California, Arizona). The subset of applications that are made aerially can also be important because the timing of harvest can be crucial to yield and quality outcomes, and aerial applications allow growers to treat more acres, more quickly, and take advantage of optimal harvesting conditions. Alternative desiccants are sodium chlorate and protoporphyrinogen oxidase (PPO) inhibitor defoliant/desiccant products such as carfentrazone, fluthiacet-methyl, pyraflufen-ethyl, and flumiclorac pentyl ester. However, none of these alternatives provide the rapid effects or rainfastness that are unique to paraquat. If paraquat were not available as a harvest aid, growers may have to wait longer between the application of a harvest aid and harvest. The longer the application window, the greater the possibility of a rain event that would further delay harvest and likely lead to reduced quality of lint, which in turn would reduce the amount the grower would be paid for their crop.

Peanuts

In peanuts, paraquat is a cost-effective, broad-spectrum herbicide effective against several target weeds that can significantly limit peanut yields when not controlled; some of the weeds targeted are redroot pigweed, Palmer amaranth, sicklepod, morning glory, Florida beggarweed, Texas panicum, and cocklebur. Paraquat offers growers flexibility in peanut weed management as it can be effectively used at multiple timings and for multiple purposes (burndown, at-plant, and post-emergence). For growers producing peanuts using conservation tillage practices, herbicide applications are necessary to 'burndown' or kill plant foliage to prepare fields prior to strip tilling and planting. Paraquat, as a broad-spectrum herbicide, targets several key weeds in peanuts at plant, so multiple alternatives would be needed to replace this use at this timing in peanuts. This would likely increase weed control costs. Paraquat is used for post-emergence control in peanuts so that weed competition is limited, and the potential for yield losses due to these weeds is reduced. In addition to its direct ability to control problematic weeds in peanuts, paraquat also has other benefits. Paraquat offers growers flexibility in soil management practices as well as crop rotation cycles as it does not have plant back restrictions between crops commonly rotated with peanuts. Without paraquat more peanut growers would likely switch from conservation to conventional tillage. Conventional tillage practices have consequences for soil management as it increases soil erodibility and decreases soil health from a loss of nutrients and organic matter. In the absence of paraquat, there would be no direct alternative, and growers would likely replace paraquat with different control strategies that are dependent on the application timing of paraquat's current use patterns. There are no chemical alternatives to paraquat for its FIFRA Section 24(c) late season use. Given this information, BEAD determined that use of paraquat has high benefits for peanut growers.[24]

[24] Coy and Kells, 2020. Paraquat Use on Peanut: Usage, Benefits and Impacts of Potential Mitigation for Registration Review. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0211

Soybeans

Paraquat is used in the spring before soybean crops emerge, as a preplant/preemergence, burndown herbicide in soybeans. It is also registered as a pre-harvest aid in soybeans however this is not anticipated to be a common use pattern in soybeans. Burndown treatments are applied any time after harvest and before planting to reduce the number of overwintering weeds and to rid the field of weeds that did overwinter. The greatest amount of paraquat usage in soybeans is for control of Amaranthus species in southern U.S. regions, for example, Palmer amaranth and redroot pigweed. It is also used for control of henbit and lambsquarters. Glyphosate resistance in Amaranthus species, especially for Palmer amaranth, is problematic and expensive for soybeans growers in the Delta region of the United States (Arkansas, Louisiana, Mississippi). Weed resistance to glyphosate has resulted in more growers using paraquat, which has a different mode of action and can control glyphosate-resistant weeds. Without paraquat, growers with glyphosate-resistant weeds in the field would have an increase in cost from having to use a combination of two or more herbicides to match paraquat's control; without paraquat, growers would also have fewer rotational partners to reduce stress on further resistance developing. To maintain an efficacy equal to paraquat, growers could replace paraquat with a combination of glufosinate and either 2,4-D or dicamba, or glyphosate and saflufenacil with 2,4-D or dicamba. In addition to its direct ability to control problematic weeds in soybeans, paraquat also has other benefits. Paraquat can be used for application under cool and wet weather conditions, and it has a relatively high rainfastness characteristic. This characteristic of paraquat allows growers a greater window of application timing without anticipating crop damage or a reduction in weed control efficacy. Given this information, BEAD determined that use of paraquat has high benefits for soybeans growers.

C. Risk-Benefit Balance: 2021 Paraquat ID

The scenarios for which EPA has identified potential remaining risks after implementation of the mitigation measures identified in the Paraquat ID are described above in Section IV.A. To determine whether paraquat could met the FIFRA standard for registration, i.e., whether these risks would not be unreasonable when taking into account the economic, social, and environmental costs and benefits of the use of paraquat, EPA carefully weighed these remaining risks against the benefits for those uses. As stated in the Paraquat ID, EPA concluded that these risks were outweighed by the benefits of the use of paraquat. In this section the Agency provides clarification of the rationale for the Agency conclusions in the Paraquat ID.

1. Use as a Cotton Harvest Aid

As part of EPA's further consideration of its risk-benefit balancing process, the Agency identified that the MOEs presented in the Paraquat ID were based on a 1.0 lb AI/acre rate.[25] However, according to currently registered labels, when used as a cotton harvest aid, paraquat is applied at a rate at or below 0.5 lb AI/acre (see Appendix A). The Agency recalculated its risk estimates based on this 0.5 lb AI/acre application rate and presents those updated numbers in Appendix A.

As discussed above, EPA has identified two exposure scenarios for which potential risks remain after mitigation from the use of paraquat as a cotton harvest aid: (1) for applicators from aerial applications and (2) to workers engaged in post-application activities such as picker operator, raker, or tramper cotton harvest aid.

As discussed in Section IV.B. above, paraquat has unique characteristics that make it desirable for use as a cotton harvest aid (boll opener/defoliant and desiccant). Cotton harvest is a time-sensitive process, one that when gone wrong can have consequences for cotton quality and grower outcomes.

In addition, the harvesting of cotton is a highly specialized process.[26,27] It requires careful consideration of the agronomic conditions and proper implementation of the chosen regimen. Moreover, it is likely to rely on specialized (and expensive) equipment. Applications of paraquat as a harvest aid are therefore, either very likely to be made by the grower himself or by professionally trained pesticide applicators as paraquat is a restricted use pesticide. Grower survey shows that 80% and 90% of cotton acres treated with a paraquat harvest aid were treated by the grower himself over the periods 2014-2018 and 2017-2021, respectively.[28] Meanwhile 11% and 5% of cotton acres treated for harvest aid use were treated with aerial applications over the same respective time periods. Risks from harvest activities (post-application exposure) would also likely be borne by the grower himself or a custom hire crew (who also may farm cotton) that owns specialized cotton harvest equipment.[29,30]

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[25] Britton, W., T. Morton, A. Wray. 2019. Paraquat Dichloride: Draft Human Health Risk Assessment in Support of Registration Review, Table 11.3.1. Occupational Post-Application Non-Cancer Exposure and Risk Estimates for Paraquat. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0121

[26] Stichler, C. J. Supak, K Hake, B Warrick. Undated. The Proper Use of Cotton Harvest-Aid Chemicals. Texas Agricultural Extension Service, Texas A&M Available at http://publications.tamu.edu/COTTON/PUB_cotton_The%20Proper%20Use%20of%20Cotton%20Harvest-Aid%20Chemicals.pdf

[27] Griffin, J. 2019. East and South Texas Cotton Harvest Aids: The Art and Science. Available at: https://agrilife.org/texasrowcrops/2019/08/02/east-and-south-texas-cotton-harvest-aids-the-art-and-science/

[28] Kynetec, 2023. The AgroTrak Study, Data Subset 2014-2018 and 2017-2021. Data collected on pesticide use for about 60 crops by annual surveys of agricultural users in the continental United States. Survey methodology provides statistically valid results, typically at the state level.

[29] Hutmacher, R. et al., 2012. Sample Costs to Produce Cotton, Pima Variety, University of California Cooperative Extension. Available at: https://cottoninfo.ucdavis.edu/files/150403.pdf

[30] Steadman, J. 2016. Harvesting Bottom Line Advantages. Cottongrower.com. Available at: https://www.cottongrower.com/cotton-production/harvest/harvesting-bottom-line-advantages/. Accessed January 2024.

Inhalation risks from aerial applications of paraquat for cotton desiccation

In its 2021 Paraquat ID, the Agency sought to address inhalation risks identified for aerial applicators of paraquat. Applicator inhalation risks are a function of amount applied in a single day (i.e., application rate per acre and acres treated in a single day).

In the Paraquat PID, the Agency proposed to cancel all aerial applications of paraquat except for cotton desiccation (harvest aid use). This would mitigate all inhalation risks to aerial application except for the cotton harvest aid use. The exception was made for the cotton harvest aid use because of its anticipated high benefits, its niche use pattern (i.e., important in only a subset of applications in a few states), and because inhalation risks to aerial applicators for the harvest aid use pattern were inherently lower than the herbicidal use (up to 0.5 lb per acre compared to up to 1.0 lb per acre when applied as an herbicide). However, after the Paraquat PID was issued, the Agency received public comments from several stakeholders that cited the importance of aerial applications of paraquat in other use sites and urged the Agency to reconsider the proposed decision and to allow additional aerial uses. The Agency considered these comments (as summarized in BEAD's response to public comments document) and determined that specific regions (e.g., Mississippi Delta) could potentially face larger impacts of cancellation of aerial use when applied as an herbicide.[31] Therefore, in the Paraquat ID, the Agency allowed but still restricted aerial application from what had previously been allowed on paraquat labels by limiting aerial applications of paraquat to 350 acres per applicator in a 24-hour period for all uses except cotton and soybean[32] harvest aid. This type of mitigation (daily acreage application limitation) is not commonly employed by the Agency. However, to recognize the benefits of use and because inhalation risks for most applicators are not of concern when applications are restricted to the daily acreage limit, this mitigation was allowed. As proposed in the Paraquat PID, the Agency decided in the Paraquat ID that it would continue to allow use of aerial applications of paraquat when applied as a harvest aid. In 2022, the Agency published an amendment to the ID which allowed soybean harvest aid use aerially without a daily acre treated limitation because when used at the lower 0.25 lb active ingredient/acre rate, risks of concerns to aerial applicators would not be expected. [33]

As such, although most patterns of paraquat applied aerially no longer resulted in a risk of concern, EPA acknowledges that potential inhalation risks (lung and respiratory effects) resulting from aerial applications for cotton desiccation remain. As reported in Table 2 above, the inhalation MOE associated with aerial application of paraquat to cotton at 0.5 lb AI/acre is 71 (LOC = 100). Aerial applicators of liquid formulated pesticides (i.e., pilots) may be exposed to these products during spraying activities, when returning to the staging area to have their spray tanks and fuel tanks refilled before another spray application, and when exiting/entering the cockpit at the staging area during fueling to make aircraft adjustments. The Agency assesses all aerial applications with the assumption that engineering controls (an enclosed cockpit) are used

[31] English, L., et al. 2021. BEAD Response to Paraquat Usage and Benefit Related Comments Received on the Preliminary Interim Decision of Paraquat. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0308

[32]Amendment to Paraquat Dichloride Interim Registration Review Decision, Case Number 0262 Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0312

[33]Amendment to Paraquat Dichloride Interim Registration Review Decision, Case Number 0262 Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0312

during spray. Although the paraquat labels do not impose a limitation on the amount of acreage that can be treated in a 24-hour time period for cotton desiccation, the Agency default of 1,200 acres is assumed to be an accurate estimate given that the National Agricultural Aviation Association reported that the usual number of acres treated for cotton with one aircraft in a day was 1,125 acres.[34]

As noted in the Paraquat ID, aerial application of paraquat is important for timely desiccation of cotton crops prior to harvest. This use is especially important among certain production regions where field sizes are significantly larger, requiring aerial application to harvest the cotton in a timely manner. Aerial and state-level use patterns, as reported in grower survey data and reported in and Hanson and Chen (2020), indicated that the impacts of prohibiting aerial application for desiccation on cotton were expected to be concentrated in certain regions. Even though aerial applications of paraquat when applied in cotton as a harvest aid represent a fraction of the overall use as most harvest aid applications are done by ground (likely using an enclosed cab), the following four states comprised most (i.e., 95%) of the cotton acres treated aerially with paraquat: Arizona, California, Louisiana, and Texas. In response to EPA's inquiry on additional specific questions related to paraquat use and grower considerations, United States Department of Agriculture, Office of Pest Management Policy (USDA OPMP) reported in May 2020 that paraquat use as a desiccant is regionally important in the high plains of Texas and into western Oklahoma.[35] The Agency also found that paraquat is predominantly used in Texas as a harvest aid.[36] USDA reported that use of stripper pickers is largely centralized in the high plains of Texas and west Oklahoma and that where stripper pickers are more predominant, more paraquat is likely to be used as a harvest aid. Syngenta also reported to the Agency during a July 2020 meeting that in west Texas, growers need to cover many acres in a short amount of time during harvest and aerial applications of paraquat make this possible. Timing is critical when harvesting cotton and proper defoliation and/or desiccation is essential to maintaining quality cotton and an efficient harvest.[37,38]

Based on the available information at the time of the Paraquat ID, EPA's understanding was that these paraquat applications would be made by certified applicators who have also taken the paraquat specific training and are therefore well versed in the risks associated with paraquat and proper precautions to safeguard themselves; in situations where application timing is critical; and predominately in specific regions. While the Agency found potential risks of concern for aerial applications above 350 acres per applicator in a 24-hour period, EPA did not consider those risks unreasonable, in light of the critical need for paraquat in cotton desiccation. Prohibiting aerial applications above 350 acres per applicator in a 24-hour period would have had significant

[34] 2019 NAAA Aerial Application Industry Survey: Operators, Table 13. Available at: https://downloads.regulations.gov/EPA-HQ-OPP-2011-0855-0204/attachment_6.pdf.
[35] USDA OPMP, 2021. USDA Response to EPA's Inquiry on Paraquat Use Patterns and Benefits in Cotton. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0306
[36] Hanson, C., and Chen, C. 2020. Paraquat Dichloride (Herbicide and Harvest Aid) Use, Usage, Benefits and Impacts of Potential Mitigation in Cotton (PC# 061601). Available at https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0213
[37] Warrick, B., C. Sansone, J Johnson. 2002. Cotton Production in West Central Texas. Available at: https://sanangelo.tamu.edu/extension/agronomy/agronomy-publications/cotton-production-in-west-central-texas/
[38] Maeda, M., W. Keeling. Texas A&M AgriLife Research and Extension. Available at: https://lubbock.tamu.edu/files/2022/08/2022-Texas-High-Plains-Cotton-Harvest-Aid-Guide-2.pdf

impacts on growers who need paraquat for cotton desiccation, which often involves larger field sizes and because the timing of harvest can be crucial to yield and quality outcomes.

Post-application dermal risks from paraquat cotton harvest aid use

EPA's HHRA identified potential dermal risks of concern associated with paraquat post application activities. In the Paraquat ID, an REI of 7 days was deemed to be necessary, which was protective of most but not all potential post application risks from paraquat use, namely, certain activities associated with cotton harvest aid. The activities that remained of concern were activities associated with cotton harvesting methods: module builder operator, module builder picker operator, raker, and tramper (MOEs of concern for 11 to 27 days after treatment). As described above, paraquat is applied at a rate at or below 0.5 lb AI/acre rather than the 1.0 lb AI/acre presented in the Paraquat ID. At a 0.5 lb AI/acre application rate, potential re-entry risk estimates of concern persist from 4 to 21 days following product application, rather than 11 to 27 days as presented in the Paraquat ID. The 7-day REI fully mitigates the risks for the 'harvesting, mechanical, module builder operator' scenario (MOE = 140; LOC = 100).

The MOEs that remain below the LOC (and thus the scenarios that present potential risk estimates of concern) at the 0.5 lb AI/acre rate and the 7-day REI are as follows:

- Harvesting, Mechanical, Picker Operator MOE = 52
- Harvesting, Mechanical, Raker MOE = 52
- Harvesting, Mechanical, Tramper MOE = 25

In order to fully mitigate the potential risks associated with the picker operator and raker activities, a 14-day REI would be needed. To fully mitigate the potential risks associated with the tramper activity, a 21-day REI would be required, both of which would essentially prohibit the use of paraquat for cotton desiccation, which is critical in certain situations.

The Agency considered the impact of a 21-day REI requirement on growers, which would render the product unusable in some situations. Any significant REI increase would impact growers ability to have timely desiccation of their cotton crop close to harvest, particularly in certain situations, such as late season use in Texas or when a poor weather event or freeze is imminent in the Mid-South.[39,40] Poor weather events such as rain and freeze can significantly impact the quality and yield of a cotton crop. Growers usually pay close attention to approaching weather systems in the time just prior to harvest and will ultimately harvest sooner if a weather event is approaching. Impacts to quality and yield could occur for both stripper- and spindle-harvested

[39] Chen and Hanson, 2020. Paraquat Dichloride (Herbicide and Harvest Aid) Use, Usage, Benefits and Impacts of Potential Mitigation in Cotton
https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0213
[40] English et al., 2021. BEAD Response to Paraquat Usage and Benefit Related Comments Received on the Preliminary Interim Decision of Paraquat (PC #061601 and 061603) Available at:
https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0308

cotton.[41,42] Timing is an important factor for the harvest aid late season use of paraquat because growers need to get in the field and harvest quickly when crop and weather conditions are optimal to maintain yields and cotton quality. Identified alternatives do not have the characteristics of rapid effects and rain-fastness that are unique to paraquat. The Agency considered the potential impact on the quality of the cotton harvested in addition to the potential increase in cost from having to use an alternative to paraquat if growers had to switch to alternative chemistries that did not work as rapidly.

The four scenarios modeled in HED risk assessments represent two cotton harvesting methods – the module builder technique and the trailer harvesting technique. The cotton harvest activities described in this section are pulled from one of the studies[43] that underlies the data used to assess post-application activities and make the conclusions found in the Agency's Occupational and Residential Registration Review Exposure and Risk Assessment.[44] The module builder technique for cotton harvesting, "included three job categories: a picker operator (PO), a module builder operator (MBO) and a raker (RK). The PO drove the mechanical cotton picker through the field to collect cotton and performed minor maintenance tasks, as necessary. When the basket on the picker became filled with cotton, it was unloaded into a machine called a module builder. This machine, which compressed the cotton by mechanical means into a large rectangular solid called a module was operated by the MBO. The RK performed such activities as raking and gathering loose cotton on the ground and servicing the picker."[45]

Additional details of the study relayed that the PO scenario captured exposures where "the worker drives and operates the picking machine with the windows and doors open. Performs minor maintenance on the pickers such as raking debris from the vents and cleaning the windshield and side mirrors." [46] These assumptions are based on the available data that EPA has currently to inform the risk assessment; however, it has been suggested that most PO equipment in use today has air-conditioned enclosed cabs, which would allow for the operation of the picking machine with the windows and doors closed.[47] If that is the case, then potential exposures could be lower than estimated.

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[41] Chen and Hanson, 2020. Paraquat Dichloride (Herbicide and Harvest Aid) Use, Usage, Benefits and Impacts of Potential Mitigation in Cotton
https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0213

[42] English et al., 2021. BEAD Response to Paraquat Usage and Benefit Related Comments Received on the Preliminary Interim Decision of Paraquat (PC #061601 and 061603) Available at:
https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0308

[43] Eberhart, D.C., G.K. Ellisor. 1993. Evaluation of Worker Exposure to Tribufos During Harvesting of Cotton Treated with DEF 6.

[44] Britton, W. 2019. Paraquat Dichloride: Occupational and Residential Registration Review Exposure and Risk Assessment. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0126

[45] Eberhart, D.C., G.K. Ellisor. 1993. Evaluation of Worker Exposure to Tribufos During Harvesting of Cotton Treated with DEF 6.

[46] Eberhart, D.C., G.K. Ellisor. 1993. Evaluation of Worker Exposure to Tribufos During Harvesting of Cotton Treated with DEF 6.

[47] Comment submitted by Steve Hensley, Senior Scientist, Regulatory and Environmental Issues, National Cotton Council (NCC). Available at: https://www.regulations.gov/comment/EPA-HQ-OPP-2011-0855-0179

The Raker scenario models an agricultural worker who rakes the cotton that falls to the sides of the module builder during the unloading process and throws the cotton into the builder using their hands and arms; cleans lint and debris out of the air filters located on the rear of the picking machine (using gloved hands) while the picker unloads the cotton into the module builder. While this practice is still used on some farms, it is a practice that is becoming increasingly less common and may be obsolete in the next decade. This is because growers are moving toward cotton pickers that simultaneously pick and build modules and eliminate the need for additional labor including a raker.[48,49,50] Any growers still using separate picker and module building systems are likely to be experienced pickers who can therefore harvest and leave few scraps for raking. The cost of hiring labor to pick up the scraps that remain using equipment in use today is unlikely to warrant the revenue received for picking up the little cotton that has been left on the field.

The Tramper scenario is a scenario that would occur only in the trailer harvesting technique, which is becoming obsolete. This scenario represented a worker physically tramping cotton into a trailer to compact the load; this trailer harvesting technique was even "becoming obsolete from an economic standpoint" when the study and report was completed in 1993. A 2016 survey of cotton growers across the United States similarly found that the use of trailers for harvesting cotton had become obsolete.[51] In the HHRA, it was reported that, "while HED will continue to present quantitative risk estimates for tramping cotton, we acknowledge that cotton harvest practice is moving increasingly toward the newer round mini module harvesters and use of trailers is becoming obsolete."

In the end, the Agency weighed the option of fully mitigating the risk through imposing a 21-day REI requirement but found that it would make paraquat unusable for cotton desiccation needs thereby eliminating the entire benefit of paraquat use against the 7-day REI requirement, which has the effect of reducing some exposure and potential risk, while also imposing some burden but not eliminating the usefulness of paraquat for growers who need it for cotton harvesting. While the Paraquat ID did not identify measures that fully mitigate the potential risks of concern associated with these few cotton harvest activities, there is some evidence to support an industry shift away from the trailer cotton harvesting technique described above. In addition, the 7-day REI is expected to reduce exposure significantly (MOEs range from 25-140 at 7 days rather than 12-67 at day 0). In light of this, the Agency determined that a 7-day REI for cotton desiccation accomplished an appropriate balancing of the risks and benefits. A shorter REI would provide even less risk reduction, but a longer REI would essentially prohibit its use for cotton desiccation, which is a critical use in certain situations.

As discussed above, EPA acknowledges that cotton harvesting technology is rapidly advancing, and use practices continue to evolve. The Agency may consider requiring label statements that

[48] Comment submitted by Roger Isom, President/CEO of California Cotton Ginners and Growers Association. Available at: https://www.regulations.gov/comment/EPA-HQ-OPP-2011-0855-0195.
[49] https://www.cottoninc.com/cotton-production/ag-resources/harvest-systems/seed-cotton-handling-storage/a-brief-history-of-cotton-modules/
[50] Roberson, 2010. Growers Compare Costs of Conventional OBMB Pickers 228382. Available online at: https://www.farmprogress.com/farming-equipment/growers-compare-costs-of-conventional-obmb-pickers-228382
[51] Comment submitted by Steve Hensley, Senior Scientist, Regulatory and Environmental Issues, National Cotton Council (NCC). Available at: https://www.regulations.gov/comment/EPA-HQ-OPP-2012-0167-0137.

prohibit tramping or raking activities when paraquat is applied as a harvest aid. The Agency is seeking comment on this or an alternate approach to addressing potential risks associated with use of paraquat as a cotton harvest aid.

2. *Groundboom applications of paraquat for many other crops, allowing high acreage use (more than 80 acres) with enclosed cabs and low acreage use (80 acres or less) with open cabs*

In its HHRA, EPA identified potential inhalation risks of concern associated with paraquat application via groundboom equipment. In order to address these risks in the Paraquat ID, EPA determined that it was necessary to require enclosed cabs for any individual making high acreage applications, which refers to applications to more than 80 acres in a 24-hour period. In addition, for paraquat applications to less than 80 acres in a 24-hour period, EPA determined that the use of enclosed cabs is needed to fully mitigate potential risks of concern. However, in an effort to provide flexibility to growers that do not have access to sprayers with enclosed cabs, EPA offered the option of applying paraquat with a PF10 respirator in open cabs. Three high acreage scenarios resulted in residual potential risks of concern with enclosed cabs (MOEs = 52, 65, and 87). Additionally, there were potential residual risks from three of the lower acreage application scenarios with PF10 respirators (MOEs = 76, 81, and 95).

Groundboom applications of liquid formulated pesticides may result in exposures to operators during spraying activities, such as driving the tractor during spray, adjusting sprayer height, adjusting/cleaning sprayer nozzles, and general interaction with the equipment. Based on current label application rates and expected exposures from these activities, the Agency identified potential inhalation risks (e.g., upper respiratory irritation) to the applicators that are of concern, i.e., the MOEs are less than the LOC. The risk estimates were higher for an individual making higher acreage applications than lower acreage applications due to higher expected exposures.

The scenarios where potential risks for growers applying paraquat to more than 80 acres of land in a 24-hour period remain even with the use of an enclosed cab include applications of 1 lb active ingredient per acre to Barley; Coniferous/Evergreen/Softwood (non-food); Corn, Field; Corn, Pop; Cotton; Fallowland; Peanuts; Peas (Unspecified); Rice; Safflower; Sorghum; Soybean; Sugarcane; Sunflower; Tyfon; 0.80 pounds active ingredient per acre to Legume Vegetables; Mint; and 0.6 pounds active ingredient per acre to Grasses Grown for Seed; and Potato, White/Irish (or Unspecified). To address these risks, EPA identified the need for enclosed cabs to reduce the exposure. Because enclosed cabs would not fully mitigate the risks for all application scenarios, the Agency conducted outreach to USDA to identify additional measures that would be feasible and provide additional protection for ground applicators, such as wearing a respirator in the enclosed cab.[52] The feedback through USDA outreach was that grower representatives reported that it would be problematic to wear a respirator while operating in an enclosed cab. Respirators were reported to be bulky and inhibit the ability of applicators to look behind themselves, therefore EPA did not pursue this as an additional mitigation option. If a grower does not have an enclosed cab, this mitigation requirement would impose costs (reduce

[52] USDA OPMP, 2021. USDA Response to EPA's Inquiry on Paraquat Use Patterns and Benefits in Cotton. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0306

benefits of paraquat use) by requiring the purchase of new equipment, hiring an applicator with the proper equipment, to switch to an alternative pesticide, or apply paraquat over multiple days.

For an individual applying paraquat to less than 80 acres, EPA required the use of enclosed cabs or PF10 respirators in open cabs. The option of applying paraquat to less than 80 acres with a PF10 respirator rather than an enclosed cab was offered to provide flexibility to growers that do not have access to sprayers with enclosed cabs. Where an individual uses an enclosed cab and applies to 80 acres or less acres in a 24-hour period, the risks are fully mitigated. If an open cab is used with a respirator, three scenarios remain of concern for the low acreage applications. These include applications to several typical field crops at 1 lb AI/acre, tobacco at 0.94 lb AI/acre, and Legume Vegetables; Sage, Clary; Taro; Vegetables (Unspecified) at 0.80 lb AI/acre (MOEs = 76, 81, and 95 respectively). The Agency considered the impacts of requiring respirators on growers—for growers who do not already have enclosed cabs or respirators, there would be costs to obtaining and maintaining equipment, undergoing training, to hiring someone to do the application who has the proper equipment, or switching to an alternative pesticide.

Although using enclosed cabs for applications to high acreage and respirators in open cabs for lower acreage applications does not fully eliminate the potential risk, the Agency determined that the need for paraquat applications to treat weeds, including those that may be prone to other chemistries, outweighed the residual risks from these application scenarios. Paraquat was found to have high per-acre benefits for several crops as an herbicide including in cotton, soybeans, and peanuts. Benefits of the use of paraquat as an herbicide are high because its unique mode of action makes it an effective tool for resistance management and targeting particularly problematic target weeds that are resistant to other mode of actions (MOAs). The Agency chose to allow continued use on all other crops for which it was labeled. While usage, in terms of the percent of crop acres treated with paraquat is low in other sites, the per-acre benefits growers obtain are likely to be similar to those of cotton, soybean and peanuts. That is, the Agency anticipated that where it is used it may be used to target problematic pests that may be resistant to other chemistries. With this analysis, EPA determined that in consideration of the benefits afforded by the use of paraquat, the remaining risks associated with paraquat groundboom application are not unreasonable.

The Agency may consider requiring enclosed cabs for groundboom application regardless of acres treated. EPA is seeking comment on the feasibility of this mitigation in addition to information regarding the usage, typical application rates, and benefits information for use sites other than cotton, soybean, and peanuts as it considers whether the benefits continue to outweigh the risks associated with groundboom application of paraquat to specific crops.

V. CONSIDERATION OF SPECIFIC ISSUES RAISED BY PETITIONERS ABOUT THE PARAQUAT ID

A. Consideration of Parkinson's Disease

EPA's standard practice for assessing risks in registration review involves consideration of the entire available database of non-guideline and guideline toxicity studies, in addition to available

literature and other publicly available data, to identify the range of possible effects for a given compound. Those studies conducted using human-relevant routes of exposure in which an adverse effect is identified are then used to identify PODs following that compound's exposure, i.e., selection of PODs is based on a given chemical's anticipated route of exposure as determined by its use pattern. Based on the use pattern for paraquat, EPA conducted acute and chronic dietary (food and water) assessments for the general population; adult (dermal) and children (dermal and incidental oral) exposure assessments resulting from spray drift; and occupational handler (dermal and inhalation) and occupational post-application (dermal) exposure assessments.

In addition to the database of guideline and non-guideline studies available for review and consideration, EPA evaluated over 200 whole animal studies from the open literature, including several of which were referred to in the Petitioner's opening brief, through application of a thorough systematic review process following current EPA practice. EPA's systematic review process, study quality evaluation, weight of evidence analysis, and conclusions are summarized in the HHRA and described in extensive detail in the PD systematic review entitled *Paraquat Dichloride: Systematic review of the literature to evaluate the relationship between paraquat dichloride exposure and Parkinson's disease* (hereafter referred to as the Systematic Review Memorandum).[53] EPA has addressed many comments and concerns, similar to those voiced by the Petitioners, regarding the EPA's interpretation of that data and information in the *Paraquat: Response to Comments (RTC) on the Draft Human Health Risk Assessment.*[54] Briefly, EPA concluded that those studies had numerous limitations or deficiencies, which are discussed further below, that led to them being considered inappropriate for POD selection.

The majority (90%) of the open literature studies investigating PD-like effects involved the test substance being directly injected into the test animals, and as such those studies are not administered via a relevant pathway, given the anticipated routes of exposure to occupational workers or the general population (i.e., through oral, dermal, and inhalation pathways). In addition, they bypass common pharmacokinetic barriers like absorption and distribution or can alter metabolism and elimination behaviors. Such changes in ADME behaviors can result in greater bioavailability, and often result in direct introduction of the test material (i.e., paraquat) to the target site that would not be otherwise possible when using the typical exposure routes (oral, dermal, and inhalation). A detailed description of the toxicokinetics for paraquat, as determined from several open literature studies, is provided in the HHRA and Systematic Review Memorandum and is summarized in part as follows. Paraquat has been shown to accumulate in the central brain (i.e., regions involved in PD outcomes) following repeat injections and single oral exposures, with tissue concentrations increasing linearly with dose (Prasad et al., 2007).[55] Paraquat can also accumulate to a small degree in the same region of the brain following repeated oral exposure, until reaching an apparent saturation point after 90 days

[53] Wray A. and Niman A., Paraquat Dichloride: Systematic review of the literature to evaluate the relationship between paraquat dichloride exposure and Parkinson's disease. Available at https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0125.
[54] Britton W. et al., Paraquat: Response to Comments on the Draft Human Health Risk Assessment. Available at https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0216.
[55] Prasad K, Winnik B, Thiruchelvam MJ, Buckley B, Mirochnitchenko O, and Richfield EK. 2007. Prolonged toxicokinetics and toxicodynamics of paraquat in mouse brain. *Environ Health Persp.* 115(10): 1448-1453.

of exposure (Widdowson et al. 1996; Minnema et al., 2014).[56,57] The available toxicokinetic data do not indicate such saturation will occur following repeat dosing via injection dosing, although it is recognized that tested concentrations are generally lower than those administered orally. The toxicokinetic and toxicodynamic data also indicate that to achieve similar adverse effects and internal brain concentrations between injection and oral administration, animals would have to be exposed to an oral dose nearly 2X to 10X the injected dose (Prasad et al., 2007; Minnema et al., 2014; Campbell et al., 2021).[58] In contrast to oral or injection administration, paraquat administered via inhalation has been shown to sequester entirely in the olfactory bulb in small amounts (Rojo et al., 2007).[59] The toxicokinetic data thus qualitatively and quantitatively support that studies administering paraquat via injection would not be appropriate to use for POD selection because of more compound being retained in tissue or being sequestered in specific brain regions that would otherwise not be targeted through oral or inhalation exposures.

As noted in the Systematic Review Memorandum, it was not possible to establish a dose-response relationship in most of the remaining 10% of open literature studies that did not use injection as a route of administration or that used an appropriate animal model, because only one dose was tested or due to other identified deficiencies. Such deficiencies included limited animal care information, inconsistencies among experimental methods across the different studies, sources of potential bias such as investigators not being blinded to treatment levels, inadequate sample sizes, and only qualitative data being reported for one or more health outcomes.

A study must be able to inform a dose-response relationship to be considered for use in identifying a POD.[60] A LOAEL and NOAEL can usually only be established for those studies that test with 2 or more doses and that demonstrate a dose-response relationship. For studies that only test one dose, caution should be taken since these studies may be impacted by experimental and biological variability that produces spurious findings rather than effects related to treatments with the test compound, which lowers confidence in the study results. However, in some cases, a study testing at only one dose can be supported by another (or other) studies as long as their experimental conditions are similar (i.e., same methods, test species, chemical purity, etc.) to the degree that dose and/or temporal trends are able to be established with confidence. UFs are then applied only after selection of an appropriate POD based on a NOAEL, LOAEL, or benchmark dose (BMD). The default UFs for interspecies and intraspecies differences are 10x each. Other UFs that may be applied/retained include the LOAEL-to-NOAEL extrapolation UF when effects are seen at the lowest dose tested in a study, the subchronic-to-chronic extrapolation factor when

[56] Widdowson PS, Farnworth MJ, Upton R, and Simpson MG. 1996. No changes in behavior, nigro-striatal system neurochemistry or neuronal cell death following toxic multiple oral paraquat administration to rats. Hum Exp Toxicol. 15(7): 583-591.
[57] Minnema DJ, Travis KZ, Breckenridge CB, Sturgess NC, Butt M, Wolf JC, Zadory D, Beck MJ, Mathews JM, Tisdel MO, Cook AR, Botham PA, and Smith LL. 2014. Dietary administration of paraquat for 13 weeks does not result in a loss of dopaminergic neurons in the substantia nigra of C57BL/6J mice. Regul Toxicol Pharm. 68(2): 250-258.
[58] Campbell Jr. JL, Travis, KZ, Clewell III HJ, Stevens AJ, Hinderliter, PM, Andersen ME, Botham PA, Cook AR, Minnema DJ, and Wolf DC. 2021. Integration of paraquat pharmacokinetic data across species using PBPK modelling. Toxicol Appl Pharmacol 417: 115462.
[59] Rojo AI, Cavada C, de Sagarra MR, and Cuadrado A. 2007. Chronic inhalation of rotenone or paraquat does not induce PD symptoms in mice or rats. *Exp Neurol.* 208(1): 120-126.
[60] See Reference Dose (RfD): Description and Use in Health Risk Assessments | US EPA, located at https://www.epa.gov/iris/reference-dose-rfd-description-and-use-health-risk-assessments.

a study of short duration is meant to represent longer-term exposures, a database UF when certain critical toxicity information is currently unavailable, or a modifying factor that may address any other scientific uncertainties for a chemical.[61] In summary, it is important to note that the application of UFs occurs after the Agency has evaluated all the available data and identified the most sensitive endpoint for a given exposure scenario in the selection of PODs. As noted above, not all studies reveal effects that are relevant for human exposure scenarios, demonstrate a dose-response relationship, or have biological and statistical significance, to name a few factors the Agency considers when selecting endpoints for assessing risks of a pesticide. Therefore, it is not appropriate nor consistent with EPA policy or practice to apply UFs to doses derived from studies that the EPA has determined are not appropriate for selection of endpoints.

EPA considered numerous lines of evidence and adhered to established risk management practices in selecting endpoints most protective of the potential exposure to paraquat from dietary sources, to bystanders, and agricultural handlers and workers. With the environmentally relevant routes (i.e., oral, dermal, and inhalation) as focus, appropriate default 10x UFs for interspecies and intraspecies differences and 1x FQPA (when applicable) were applied to PODs to achieve a total LOC of 100, with no additional UFs. The dietary, oral, dermal, and inhalation PODs were based on the most sensitive effects in the paraquat toxicity database available to EPA and were derived from studies demonstrating clear dose-response relationships.

Petitioners suggest that EPA apply an additional 10-fold UF to account for the extrapolation from a LOAEL to a NOAEL based on effects observed in open literature animal studies at a given dose (i.e., 7.2 mg ion/kg/day). As noted above, EPA examined the available information to identify the appropriate endpoints for assessing expected exposure from paraquat that would be relevant for human health effects, and then applied the appropriate UFs. EPA does not believe it is appropriate to apply the UFs to the effects in the open literature studies because those effects would not be a proper basis for POD consideration due to deficiencies, issues, and/or limitations with those studies, as discussed in further detail in the Systematic Review Memorandum. Even if those studies were appropriate, only two of the referenced animal studies, Ren *et al*., (2009)[62] and Lou *et al*. (2016)[63], identified PD-related effects at 7.2 mg ion/kg/day via the oral route. While the Lou *et al.*, (2016) study was evaluated qualitatively by the EPA, that study could not be used quantitatively despite testing at more than one dose because correspondence with the authors indicated they were unable to analytically verify concentrations of the dosing solutions during the study. However, even within this flawed study, no effects were noted at the nominal dose of 3.6 mg/kg/day, which indicates retention of a LOAEL to NOAEL extrapolation UF would have been inappropriate, even if this study were otherwise useful for identifying the POD.

EPA's currently selected PODs are much lower than the dose associated with outcomes considered PD-like hallmarks in the literature following single or repeat oral exposures.

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[61] These UFs are incorporated into the FQPA safety factor to address concern regarding prenatal and postnatal toxicity, and thus references to the FQPA safety factor can encompass a variety of UFs. *See* U.S. EPA, Determination of the Appropriate FQPA Safety Factor(s) in Tolerance Assessment (Feb. 28, 2002); https://www.epa.gov/sites/default/files/2015-07/documents/determ.pdf.

[62] Ren JP, Zhao YW, and Sun XJ. 2009. Toxic influence of chronic oral administration of paraquat on nigrostriatal dopaminergic neurons in C57BL/6 mice. *Chin Med J.* 122(19): 2366-2371.

[63] Lou D, Wang Q, Huang M, and Zhou Z. 2016. Does age matter? Comparison of neurobehavioral effects of paraquat exposure on postnatal and adult C57BL/6 mice. *Toxicol Mech Method.* 26(9): 667-673.

Exposure from inhalation is expected to result in negligible concentrations in brain regions associated with PD. Inhalation risks of concern, established from an inhalation POD of 0.0026 mg ion/kg/day, were based on portal-of-entry effects in the larynx from a route-specific inhalation study that occurred at concentrations over 2 orders of magnitude lower than the lowest concentrations eliciting neuropathological or behavioral changes considered PD-like hallmarks in published oral studies in male mice[64], even when UFs are not applied. Brain tissue concentrations arising from single or repeat dermal exposure are unknown. Although repeat dermal exposure can damage the integrity of the skin and result in increased permeability of paraquat, the external concentrations required to reach this level of damage would likely manifest first as extreme irritation due to its corrosive nature. The dermal POD (6 mg ion/kg/day) was the highest dose tested in a 21-day dermal toxicity study in rabbits. When compared to dermal equivalent doses based on oral exposures seen to elicit neuropathological and/or behavioral changes in male mice, the dermal dose is over 20X lower, and nearly 8X lower when accounting for differences in species body weights between mice and rabbits.[65] Furthermore, this dermal POD is conservative because no systemic toxicity could be evaluated above this dose due to slight to severe skin damage observed at 2.6-6 mg ion/kg/day and because of greater acute dermal sensitivity in rabbits relative to that in rats. As skin irritation effects are not typical endpoints used by EPA in risk assessments for conventional pesticides, a dermal endpoint would typically not be selected. However, in the case of paraquat, the highest dose was selected from this study to be protective of systemic toxicity at higher dermal doses after accounting for the potential of the dermal barrier to erode at higher concentrations. As a result, similar to the inhalation risks identified, dermal risks of concern were also therefore based on portal of entry effects. These PODs based on portal-of-entry effects in the skin and respiratory system from the route-specific studies are protective of systemic toxicity, including effects considered to be PD-like hallmarks in the literature observed at higher concentrations in animal models, especially when applying the default 10x UFs for interspecies and intraspecies differences to those selected PODs. This, and the toxicokinetic observations that indicate concentrations in the brain resulting from human relevant routes of exposure are likely to be insufficient for PD-like health outcomes, support the EPA's conclusion that evaluation of dermal and inhalation hazards is protective of PD-like effects.

B. Consideration of Respiratory and Dermal Risks Remaining After Implementation of Paraquat ID Mitigation and Concerns about Potential Chronic Exposures

As discussed above in Section IV, EPA recognizes that the Paraquat ID does not identify mitigations that fully mitigate all potential risks of concern from paraquat pesticide use. Risk

[64] For the purposes of this discussion only (i.e., no calculations conducted in the human health risk assessment for paraquat), the oral dose of 7.2 mg ion/kg/day was extrapolated to an inhalable dose (2.1 mg ion/kg/day) based on an estimated 3-4X higher bioavailability from the inhalation route than oral route (i.e., higher absorption through inhalation) according to toxicokinetic data in rats after different routes of administration, as discussed in Chui Y-C, Poon G, and Law F. 1988. Toxicokinetics and bioavailability of paraquat in rats following different routes of administration. *Toxicol. Ind. Health* 4(2): 203-219.

[65] For the purposes of this discussion, the oral dose of 7.2 mg ion/kg/day was extrapolated to a dermal dose (144 mg ion /kg/day) using a dermal absorption factor of 0.3% and corrected for low oral absorption (6%). A similar calculation was performed when allometric scaling was used to determine the estimated oral dose of 2.28 mg ion kg/day in rabbits by applying a body weight of 0.025 kg for mice and 2 kg for rabbits.

estimates for some exposure scenarios (certain applications for cotton desiccation and groundboom applications for other crops) still exceed the Agency's LOC. Exceeding the Agency's LOC means that the amount of exposure EPA estimates to occur in that scenario exceeds the margin of safety built around the dose at which no adverse effects were observed. This is a conservative approach that accounts for uncertainties in extrapolating from animal studies, variations in sensitivities, and the dose at which adverse effects may start to occur, in trying to protect for exposure to sensitive individuals. Additionally, conservative assumptions are often used which lead to high-end estimates of exposure (e.g., 100% crop treated and maximum estimated drinking water concentrations for dietary exposures and maximum application rates for occupational exposures). For paraquat, the risk estimates indicate the potential for respiratory and dermal effects, such as throat irritation or skin irritation. However, as noted above, the selected PODs to assess dermal and respiratory risks are much lower than the dose anticipated to lead to PD-like outcomes following single or repeat oral exposures (8X lower to over 100X lower). Notwithstanding these potential portal of entry effects, after carefully weighing these risks against the estimated benefits of the pesticide, EPA has concluded that these risks arising from dermal and inhalation exposures are not unreasonable.

Regarding concern of long-term exposure to low levels of paraquat, exposure durations for assessment are determined by considering the exposed population, the use site, the pest pressure triggering the use of the pesticide, and cultural practices. According to the current registered label directions for paraquat, applications may be conducted as pre-plant, pre-emergence, at plant, or post-emergence for the control of weeds and grasses in agricultural and non-agricultural areas; as a desiccant/harvest aid; or a post-harvest desiccant for a season. Based on this use pattern, there is the potential for short- and intermediate-term occupational exposures and short-term non-occupational bystander exposures. EPA considers "short-term exposure" to refer to continual pesticide exposure over the course of one to 30 days and "intermediate-term exposure" to refer to 30 days to six months of continual pesticide exposure. Although workers may handle or apply paraquat year after year, this does not represent continuous long term or chronic exposure to paraquat but rather represents a series of short- or intermediate-term exposures given the seasonal application timing of paraquat. Long-term exposures are continuous exposures over the course of 6-months or greater, and agricultural operations for paraquat based on registered label directions, including use sites and restrictions for the maximum number of applications per year or season, do not indicate long-term exposure to paraquat should be expected for workers or bystanders.

Because long-term (i.e.; chronic) occupational exposure to paraquat is not expected, EPA did not quantitatively assess those exposures, consistent with EPA's policy and exposure duration paradigm for long-term occupational exposures. In addition, the toxicological profile for paraquat indicates that the dermal and inhalation short-term studies and effects used to quantify risk have been selected to be protective of other systemic effects. Nevertheless, out of an abundance of caution and because of hypothesized connections between paraquat and PD, EPA considered the extensive availability of epidemiological data, as well as explored the potential for toxicological effects following chronic exposure within the systematic review of the epidemiologic literature on paraquat exposure. EPA concluded that weaknesses within and across the epidemiological, whole animal, and *in vitro* data, in addition to the exposure considerations outlined above, indicate that the weight of evidence is insufficient to link paraquat

exposure from pesticidal use of EPA registered products to PD in humans, based on the data EPA has reviewed in preparing this document.

First, it is recognized that no guideline studies were designed to evaluate PD-like hallmarks, and so no specific investigations into dopaminergic neuron health were conducted using more in-depth or robust testing methods and neurochemistry evaluations. This lack of data specific for evaluating PD-like hallmarks in whole animal studies following chronic exposures introduces some uncertainty when characterizing the impact of long-term exposure to paraquat on nervous system tissues. However, there is a lack of evidence demonstrating changes in behavioral signs or neuropathology across multiple species in any of the reviewed studies. The only clinical signs that were observed in a guideline acute neurotoxicity study and in guideline developmental studies in rats and mice were due to severe stress to the animal and often resulted in death; no neuropathology or changes in motor activity were observed. The observations in the guideline acute neurotoxicity and developmental toxicity studies were attributed to bolus dosing via gavage (i.e., one large immediate dose as opposed to smaller doses sustained over time via dietary administration) rather than neurotoxicity. Neurotoxicity was also not observed at sublethal chronic doses in at least four chronic oral studies available for paraquat. These studies are designed to evaluate the effects of a chemical throughout the entirety of the animal's adult life, thus mimicking daily dietary exposure over the lifetime of a human individual. The adverse effects identified in those studies ranged from ocular opacity to mortality at doses between 4 and 15 mg ion/kg/day. Dermal and inhalation chronic studies are typically not conducted, and so a chronic oral study can be used as a surrogate for those exposure scenarios when use patterns for a given compound suggest a potential for long-term continuous exposure (*i.e.,* pet spot-on products). It would be inappropriate to select a chronic inhalation or dermal POD to represent seasonal exposure scenarios for paraquat because those exposure patterns are not continuous. Therefore, the selected dermal and inhalation PODs based on the most sensitive portal of entry effects are the most appropriate for short-term and intermediate-term dermal and inhalation exposure scenarios, as those PODs are relevant for the evaluation of short- and intermediate-term occupational exposures and short-term non-occupational bystander exposures to paraquat.

Second, based on a weight of evidence analysis, EPA concluded that protecting for portal of entry toxicity (i.e., dermal and inhalation exposure) would also be protective of systemic effects, including but not limited to, potential putative PD-related effects or hallmarks. As noted in Section V.A. above, this conclusion was based on a number of factors, including paraquat's irritating nature and toxicokinetic profile. Higher concentrations were unable to be tested in the *in vivo* dermal toxicity study in rabbits due to animal welfare concerns arising from slight to severe skin damage observed at relatively low doses. Additionally, inhalation is a more sensitive route of exposure than the oral route in both acute (Toxicity Category I and II, respectively) and repeated dose studies with paraquat, and paraquat is moderately to severely irritating to mucous membranes (Toxicity Category II for eye irritation), leading to portal of entry effects in the upper respiratory tract from repeated inhalation. Such irritating effects would result in self-limiting exposure. As noted in the Systematic Review Memorandum, absorption from all routes is low. Paraquat is poorly absorbed across intact skin (0.3% dermal absorption), and dermal exposures are unlikely to be sustained over a chronic timeframe due to the mild to severe skin damage, including scabbing, ulceration, and seepage observed even at low doses. While data indicates that absorption and bioavailability of paraquat is highest from inhalation among the three

environmentally relevant routes (Chui et al. 1998), the toxicokinetic profile also suggests that little to no paraquat will sequester in the regions of the brain associated with PD-like health outcomes following inhalation exposure, as it was seen to distribute solely to the olfactory bulb rather than the nigra striatal region of the central brain (Rojo et al. 2007).

Petitioners suggest that there are several studies indicating that low-level chronic exposure [to paraquat] significantly increases the risk of PD. These include the epidemiologic study findings from the Parkinson's Environment and Genes (PEG) Study in California's Central Valley (Ritz et al. 2009; Costello et al. 2017), a nested case-control study of the Agricultural Health Study (AHS) cohort (Tanner et al. 2011), and a case-control study conducted in Taiwan (Liou et al. 1997). EPA has reviewed these studies and the others above in its EPA's evaluation of the available epidemiologic evidence in its Systematic Review Memorandum. As discussed below, while there are some epidemiologic studies that reported a positive association between paraquat and PD, EPA has determined that the overall body of epidemiologic evidence was too limited and insufficient to conclude that there is such a positive association.

For example, Petitioners highlight that the publication Tanner et al. (2011) reported a positive association between self-report of paraquat use and PD in the AHS cohort but did not take into account other AHS publications that reported mixed results that were inconclusive with respect to the association between paraquat and PD in the AHS cohort. AHS is a federally funded study that enrolled participants in 1993-1997 and includes more than 50,000 licensed private (farmer) and commercial pesticide applicators from Iowa and North Carolina. AHS investigators collected information on their cohort through surveys that were administered separately in 1999-2003, 2005-2010, and 2013-2015 to evaluate cancer and non-cancer endpoints, including PD. EPA's evaluation considered the totality of available epidemiologic evidence from the AHS, including six AHS publications that were available when EPA's evaluation was conducted. Based on this more complete review of AHS study findings, EPA concluded that the AHS reported conflicting results on the association between self-reported paraquat use and PD in related publications by Kamel et al. (2007) and Tanner et al. (2011). EPA's evaluation also included an additional follow-up study on the AHS cohort by Shrestha et al. (2018) that reported no evidence of an association between self-reported paraquat use and dream-enacting behavior, a common precursor to PD, and further contradicts the AHS findings from Tanner et al. (2011).

Similarly, EPA's systematic review included evaluation of eight related epidemiologic publications of the PEG study in California's Central Valley. Despite using the same study population and underlying data, EPA concluded that altogether the PEG studies reported mixed results (*i.e.,* some reported evidence of a positive association and others reported no evidence of an association) based on different measures of exposure and consideration of co-exposure to other pesticides. EPA's evaluation of the PEG study noted limitations in the exposure assessment approach because paraquat exposure was assessed indirectly using residential and workplace proximity to agricultural land (i.e., 500m distance between residential/workplace address and agricultural land). This approach has not been validated and may have limited ability to investigate exposure to paraquat specifically, rather than general residential/workplace proximity to agricultural land in the three counties of interest.

There is also additional epidemiologic information on paraquat published after EPA's evaluation and described in HED's RTC on the Paraquat ID (Britton, W. *et al*., D461689, 22-Jun-2021). As

summarized in HED's RTC, EPA evaluated updated AHS findings on the relationship between pesticide use and PD in farmers from North Carolina and Iowa (Shrestha et al. 2020). Notably, the updated study used a prospective design and an additional 15+ years of follow-up of study participants but did not replicate the earlier findings reported by Tanner et al. (2011) that are highlighted by the Petitioners.

C. Consideration of Drift Exposures

For purposes of clarifying the discussion in the next two sections, EPA is explaining how it uses several terms relevant to how people may be exposed to pesticide residues during application on or off the application site. EPA considers direct exposures to be inhalation of the spray plume or direct contact with spray (bystander or worker coming into direct contact with the spray plume) during application. Because the paraquat label prohibits the applicator from applying the pesticide in a way that would result in the spray plume coming into contact with workers or bystanders, EPA does not assess inhalation exposures to workers or bystanders; the only person who should potentially be exposed if the label language is being complied with is the handler or applicator. Indirect exposures from pesticidal applications are the result of off-target movement of pesticide sprays (*i.e.,* spray drift) that may deposit on surfaces where contact with residues can eventually lead to indirect exposures after an application (*i.e.,* children playing on lawns where residues have deposited next to treated fields). An indirect exposure would occur dermally or through non-dietary incidental oral ingestion (predominantly from hand-to-mouth behaviors in young children), which occur indirectly through contact with impacted areas, such as residential lawns. These direct and indirect (i.e., drift) exposures are also distinguished from exposures resulting from volatilization. While this is discussed in the next section, volatilization occurs after the application has been completed and the residues of the pesticide that have landed on surfaces (e.g., foliage, turf) may change to a vapor or gaseous state due to chemical characteristics and then travels through the air from the application site to other offsite areas. This section focuses on EPA's consideration of indirect exposures to paraquat through spray drift.

In the HHRA, the Agency identified potential bystander spray drift risks of concern—dermal risks for adults and combined dermal and incidental oral risks for children ages 1 to less than 2 years of age. Again, EPA did not consider the potential for inhalation risks to bystanders because compliance with label language would preclude such exposures. The Paraquat ID indicates that the dermal and incidental oral risks would be fully mitigated once the identified mitigation measures were adopted by the registrants, which they did in 2022 by submitting compliant label amendments. The mitigation measures identified in the Paraquat ID to mitigate drift concerns included: a residential area drift buffer for all aerial applications (75 feet for applications of more than 0.6 lb cation/acre, 50 feet for applications of 0.6 lb cation/acre or lower); maximum release height of 10 feet above the ground or vegetative canopy (unless a greater application height is required for pilot safety) for aerial applications; maximum release height of 4 feet above ground or crop canopy for groundboom applications; medium or coarser droplet size requirement for ground and aerial applications; applicators may not spray during temperature inversions, and applications may not occur if wind speeds exceed 10 miles per hour at the application site.[32]

[32] Paraquat 2021 ID, Available online: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0307

As part of registration review, EPA reviewed the reported incidents of paraquat exposure and found some paraquat incidents resulted from bystander exposures to paraquat. However, as reported in its Tier II Human Incidents Report,[66] the Agency found paraquat drift-related incidents to be infrequent and of low severity. No large paraquat drift events involving multiple individuals were reported. Specific incident scenarios are provided in Appendix B along with additional information about the Agency's systematic review processes on incidents. Across all the databases reviewed from 1998 to 2018, thirteen incidents involving bystanders were reported related to drift.[33] All were classified to be of low severity meaning that the person alleged or exhibited some symptoms, but they were minimally traumatic, the symptoms resolved rapidly and usually involved skin, eye, or respiratory irritation. In the case of paraquat, 9.3 million total acres were treated on average annually with paraquat in the United States between 1998 and 2018.[34] Comparatively, the number of reported incidents represent a very low percent of the overall applications of paraquat made each year, especially when considering these incidents are based on reports over a 21-year period from 1998 to 2018.

Pesticide product labels provide critical information about how to handle and use pesticide products safely and legally. Unlike most other types of product labels, pesticide labels are legally enforceable, and all carry the statement: "It is a violation of Federal law to use this product in a manner inconsistent with its labeling." The current label language specifically prohibits (1) an applicator from applying paraquat (or any other pesticide) in a way that will contact workers or other persons either directly or through drift, (2) anyone other than appropriately trained and equipped handlers to be in the Application Exclusion Zone (AEZ) during application, and (3) use of paraquat in residential or public recreational settings (e.g. homes, home gardens, schools, recreational parks, golf courses, and/or playgrounds. As a result of these label requirements, EPA expects that exposures to the application spray plume are a result of misuse, and EPA does not generally quantitatively assess the potential illegal usage of pesticide products.[67]

Although EPA has articulated concerns about the adequacy of the "do not contact" language in the past. EPA made those statements as a basis for supporting the additional requirements for the AEZ, which supplements the protections provided by the "do not contact" requirement. *See* Pesticides; Agricultural Worker Protection Standard Revisions, Final Rule, 80 FR 67496 (2015).[68] The AEZ goes beyond the "do not contact" requirement by establishing an enforceable

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[66] Evans, E et al, 25-July-2018; D446902 Paraquat: Tier II Human Incident Report

[33] The Agency does not typically provide total incident numbers across databases as there may be duplication of incidents across databases.

[34] Kynetec USA, Inc. 2021a "The AgroTrak® Study from Kynetec USA, Inc." iMap Software. Database Subset: 1998-2016. [Accessed October 2023].

[67] Britton W. et al., Paraquat: Response to Comments on the Draft Human Health Risk Assessment. Available at https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0216.

[68] Although EPA finalized a rule in 2020 that sought to roll back some of the protections from 2015 WPS rule establishing the AEZ, the 2020 rule has never gone into effect due to a preliminary injunction issued in response to litigation challenging the 2020 rule. As a result, the 2015 final rule and its provisions related to the AEZ are still in effect and enforceable. *See* Pesticides; Agricultural Worker Protection Standard Revisions, Final Rule, 80 FR 67496 (2015). Further, in February 2023, EPA published a proposed rule seeking to reinstate certain AEZ requirements that would be impacted by the 2020 rule, including: 1) the requirement that pesticide handlers suspend applications if any worker or other person, other than appropriately trained and equipped handers involved in the application, enters the AEZ regardless of whether they are on or off the establishment; 2) the requirement that pesticide handlers

25 to 100-ft buffer between the application equipment and persons who may enter the area during application and requires the handler to immediately suspend application upon a person entering the AEZ, regardless of whether that person is within the boundary of the agricultural establishment. Those very requirements apply to any pesticide product label referencing the WPS, including paraquat. The Paraquat ID took into account all protections afforded by the WPS, including the AEZ. For a detailed description of the AEZ, see Appendix B.

Mitigation measures from the Paraquat ID, EPA policy, and the WPS are evidence-based actions primarily intended to reduce the risks of illness or injury to bystanders, workers, and handlers resulting from occupational application of pesticides used in the production of agricultural plants on agricultural establishments (*i.e.,* farms, forests, nurseries, and enclosed space production facilities, such as greenhouses).

D. Consideration of Exposures from Volatilization and Dust

EPA considered several factors when reviewing the potential for indirect inhalation exposure caused by volatilization of deposited paraquat from previously treated fields. While the volatilization screening tool is one piece of information to help illustrate volatilization potential, chemical-specific air monitoring data, physiochemical properties, temperature, wind speed and direction, and application parameters are all impactful in considering if a specific chemical will likely volatilize and drift from a treated field. Based on the results of an ambient air monitoring study from the California Air Resources Board (CARB), EPA concluded that paraquat is not expected to volatilize from previously treated fields and thus, EPA has adequately accounted for the potential for exposures to bystanders from volatilization.

The CARB monitored for air concentrations of paraquat equal to or greater than 0.022 µg/m^3 in communities near agricultural areas and did not find detectable levels of paraquat. CARB conducted ambient air monitoring to measure outdoor air concentrations of paraquat four days a week from August 31 through November 5, 1987, at four sites (*i.e.,* at schools) in Fresno County near agricultural areas expected to receive applications of paraquat and scheduled to coincide with applications to cotton.[69] According to the described study methods at the time, air monitoring is completed in high use counties during peak season usage for the pesticide under evaluation. All of the 318 samples analyzed for paraquat were less than the minimum limit of detection (LOD) of 0.022 ug/m^3 for a 24-hour sample.[70] Based on the results of the study, no bystander post-application inhalation exposures would be expected from volatilization following applications of paraquat to cotton. EPA noted in the HHRA that the CARB ambient air monitoring data has several uncertainties. More specifically, EPA noted that the older study may not be reflective of current agricultural practices and is limited to a single geographic area and

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suspend applications if any worker or other person, other than appropriately trained and equipped handers involved in the application, enters the AEZ regardless of whether they are in an area subject to an easement; and 3) the requirement that the AEZ extend 100 feet for ground-based fine spray applications and extend 25 feet for ground-based applications using medium or larger droplet sizes sprayed above 12 inches (*see* EPA-HQ-OPP-2022-0133-0002). The Agency is currently engaged in the rulemaking process and intends to finalize its proposal in 2024.

[69] Available online: https://www.cdpr.ca.gov/docs/emon/airinit/community_monitoring.htm

[70] State of California. Summary of Assembly Bill 1807/3219. Pesticide Air Monitoring Results Conducted by the California Air Resources Board 1986-1995.

crop. However, the uncertainties do not invalidate or limit its usage for risk assessment. Thus, EPA used this field data to support the risk assessment.

Consistent with its guidance, EPA had also conducted a volatilization screening analysis of paraquat. The Volatilization Screening Tool estimates the level at which residues of the pesticide may be concentrated in the air from volatilization which is then compared to a threshold level or air concentration of concern (COC) (*i.e.,* the POD divided by the total UFs); the rate at which a pesticide may volatilize from a treated field; and the air concentration at different distances from the treated field to determine potential bystander inhalation risks. The results from the screening tool present estimated air concentrations for four different crop height scenarios that are labeled as bare soil (prior to or at planting), cole (3 ft or less), row (6-18 ft), and orchards (greater than 18 ft); and field sizes for each crop scenario ranging from 10-120 acres. Screened pesticides with an air concentration equal to or lower than the COC are not expected to result in bystander risk from volatilization. Air concentrations above the COC for any crop scenario of any field size does not necessarily indicate that the active ingredient poses an inhalation risk of concern due to volatilization. Rather, due to the purposely conservative nature of the screening analysis, it may result in the EPA requesting volatilization data, route-specific inhalation toxicological data, flux studies, or any other study that would assist in refining the analysis for a more robust risk determination.

The Volatilization Screening Tool uses:

- Vapor pressure, solubility, the soil organic carbon-water partitioning coefficient (K_{oc}), and application rate to predict the rate at which a chemical volatilizes off of a treated field (*i.e.,* flux);
- Chemical-specific human health toxicological data to estimate potential bystander inhalation risks; and
- The AERSCREEN[71] model to estimate air concentrations at different distances from a treated field.[72]

The original volatilization screen for paraquat estimated air concentration above the COC (10 $\mu g/m^3/100 = 0.1\ \mu g/m^3$) for cole and row crops.[73] This screen was conducted in conjunction with EPA's posting of the Human Health Bystander Screening Level Analysis Volatilization of Conventional Pesticides on March 26, 2014, for public comment. The docket containing this

[71] The Volatilization Screening Tool uses the results of several AERSCREEN runs as its underlying basis. AERSCREEN is a screening model based on AERMOD, which is an air quality model that quantifies air dispersion based on planetary boundary layer turbulence structure and scaling concepts, including treatment of both surface and elevated sources, and both simple and complex terrain. For simplicity, the fields in AERSCREEN were modeled as squares and the sizes were limited to five values. While this may not reflect real-world agricultural practices, the sizes and shape should be adequate for screening-level purposes.

[72] Human Health Bystander Screening Level Analysis: Volatilization of Conventional Pesticides (draft March 1, 2014), located at https://www.regulations.gov/document/EPA-HQ-OPP-2014-0219-0002.

[73] This screening information is captured in one of the appendices that were released for public comment in connection with the Agency's draft volatilization guidance. Available online: Appendix C: Data Entry Sheets for the Registration Review Chemical Volatilization Screening Analysis, at https://www.regulations.gov/document/EPA-HQ-OPP-2014-0219-0005

guidance document included the Volatilization Screening Tool and Analysis,[74] which detailed the method and results for estimating volatilization. As with all active ingredients evaluated by EPA during the Registration Review process, the screening tool results are not part of the standard risk assessment but were reviewed as a standalone screening effort.[75] While the original screen previously indicated that additional data would be needed for paraquat, those results do not necessarily indicate that the active ingredient poses an inhalation risk of concern due to volatilization. Rather, due to the purposely conservative nature of the screening analysis, it may result in the EPA requesting volatilization data, route-specific inhalation toxicological data, flux studies, or any other study that would assist in refining the analysis for a more robust risk determination.

On January 18, 2024, EPA received new information about paraquat's vapor pressure, which could impact the Agency's volatilization screen results and ecological analysis of paraquat's environmental fate as well as the Agency's conclusions about the potential for exposures from volatilization. Due to the late submission, EPA has not had sufficient time to evaluate and incorporate this information into this response; however, the Agency will consider the new data and any impact on the paraquat volatilization analysis as it moves forward with its ongoing work to finalize this document by next January 2025.

EPA also further considered the issue of potential inhalation risks from the inhalation of paraquat-containing dust, which the Agency does not expect to be significant. Post-application inhalation exposures to pesticides contained within a dust particle may occur when the soil from a field previously treated with a pesticide is disturbed and the soil-pesticide bond is resuspended as dust into the air and inhaled. The potential for inhalation exposure to the pesticide within the dust is dependent on the atmospheric conditions at the time of the disturbance to create the dust, the particle size of the dust produced by the disturbance, soil characteristics, physiochemical properties of the pesticide and soil, and the bioavailability of the pesticide within the dust (i.e., the release of the pesticide from a medium (soil) and absorption by an organism). In contrast, exposures from pesticide aerosols (e.g., during handling activities), vapors (e.g., volatilization), or deposited residues (e.g., from spray drift) do not require desorption from a medium and therefore are expected to have a greater exposure potential.

Occupational post-application inhalation exposures from the resuspension of dust are considered during the assessment process. Occupational exposures to paraquat from handling activities (*i.e.,* mixing/loading, application, and mixing/loading/application) usually in liquid form are expected to be greater when compared to the potential exposures to dusts resuspending following an application. Therefore, the assessment of the inhalation exposures from the occupational handling of paraquat products are expected to result in higher exposure and risk than the potential inhalation exposure from dust resuspension following an application which are not believed to be a significant exposure source (Britton, W et al, 24-SEPT-2020; D456000).

[74] Available Online: Draft Guidances: Pesticides; Consideration of Volatilization in Pesticide Risk Assessment at https://www.regulations.gov/document/EPA-HQ-OPP-2014-0219-0001
[75] Available Online: Appendix C: Data Entry Sheets for the Registration Review Chemical Volatilization Screening Analysis, at https://www.regulations.gov/document/EPA-HQ-OPP-2014-0219-0005

The non-occupational bystander inhalation exposure assessment addresses exposures to bystanders from volatilization. The resuspension of dust generated during post-application activities entering into the air and drifting from the agricultural area is not considered a major exposure pathway to bystanders due to the number of factors mentioned above. Volatilization and contact with spray residues that have deposited off target are expected to present a greater exposure risk to paraquat than the potential contact from dust drifting from a field previously treated with paraquat, and thus, EPA considers those risk estimates to be protective of post-application exposures from paraquat dust.

For potential take-home exposures from paraquat dust residues, the WPS addresses risk management actions to protect bystanders and workers from take-home exposures due to post-application dust generating activities through education, outreach, and training requirements. The revised WPS specifically focused on expanding worker and handler pesticide safety training to include more information on how to reduce take-home exposures such as: instructions on washing before touching family members, removing soiled work boots or shoes before entering the home, washing clothes that may have pesticide residues on them before wearing them again and separately from other family clothes, keeping family members away from treated areas, and information on the potential risks to children and pregnant women from pesticide exposure.[76] *See* 40 CFR 170.401(c)(3). These provisions apply to the application of paraquat through labeling that requires compliance with the WPS.

E. Consideration of International Maximum Residue Limits (MRLs)

Foreign import restrictions on commodities treated with a pesticide can impact the benefits a grower might expect to receive from a pesticide; to the extent the restrictions impose a burden on the grower, this burden can be taken into account as a reduction in the benefit of the pesticide. As a general matter, EPA's assessment of benefits, including prices growers can receive for their treated commodities, already incorporates outside market forces, e.g., pre-existing restrictions on imports of treated commodities, and the same applies to paraquat. EPA's 2020 benefit assessments already account for the impact of pre-existing foreign MRLs on the benefits of paraquat. EPA analyses are based on revenues obtained by growers, and EPA observed no difference in price received for commodities treated with paraquat compared to other conventionally produced commodities that were not treated with paraquat.

Regarding Thailand's new import restriction on paraquat-treated commodities specifically, implemented via a maximum residue limit (MRL) of zero, EPA concludes that it does not result in any changes in the estimated benefits of the use of paraquat by U.S. producers of these commodities. For the Thai import restriction to reduce the benefits of using paraquat, it would have to either depress the price of commodities produced with the use of paraquat relative to the price of commodities produced without paraquat, or it would have to impose a fixed cost on growers who use paraquat.

The primary exports of U.S. farmers to Thailand are soybeans and wheat. There is no evidence available to indicate that growers producing paraquat-treated wheat and soybeans receive a price

[76] Agency Response to CHPAC Recommendations on Take-Home Pesticide Exposure 12-MAY-2023 (https://www.regulations.gov/document/EPA-HQ-OA-2023-0030-0003)

penalty for their crops. Thailand makes up a small portion of the total demand for U.S. soybeans and wheat, and the majority of U.S. soybeans and wheat are not treated with paraquat; therefore, Thai importers would easily be able to find sufficient commodity available to certify as untreated and purchase for use and consumption within Thailand. U.S. growers who use paraquat, meanwhile, can target their products to either domestic consumption or sales to the rest of the world; again, as the Thai ban only restricts sales of paraquat-treated commodities from a small portion of the world market, growers who use paraquat would not have difficulties finding purchasers for their commodities at the world price. While there may be costs to certifying that a commodity is untreated, based on a report provided by USDA's Foreign Agricultural Service, Thai purchasers, not U.S. growers, bear these costs.

For further information on the impact of the Thai MRL and of existing MRLs on the benefits of paraquat for U.S. growers, see Appendix C.

F. Consideration of Health-Care Costs

On the issue of monetizing human health and environmental costs, EPA refers to Section III. above, which describes OPP's risk-benefit analysis and explains why it is not necessary for the Agency to tabulate 'costs' of pesticide use in monetary terms. In OPP's analyses, the primary 'costs' (or the potential downsides of the pesticide use) are reflected in EPA's assessment of the risks to human health or the environment from use of the pesticide. Those risk estimates are expressed in terms of the potential for a particular use to pose a risk to a set of individuals or nontarget organisms. As discussed above, EPA is able to use these risk estimates in comparison with benefits to make determinations about appropriate risk mitigation measures and whether the pesticide meets the FIFRA standard for registration. FIFRA does not dictate how EPA measures costs or risks, only that it must assess whether any risks are unreasonable, while taking into account the economic, social, and environmental costs and benefits of the use of the pesticide. Per EPA guidance, "if important costs or benefits categories cannot be expressed quantitatively, they should be discussed qualitatively."[77]

There is no FIFRA requirement to express the risks to human health monetarily, and given the current risk assessment data and methodologies, doing so would not be likely to assist OPP with its decision making under FIFRA. Measuring costs of a pesticide's use in terms of the human-health related medical costs that would occur following exposure to a pesticide would simply be a different expression of the same downsides of the pesticide use, which EPA already measures through its risk assessments. The Agency assesses human health 'cost,' through assessing the 'risks' of a pesticide's use. Non-dietary human health risks are calculated using margins of exposure (MOEs) while the environmental and ecological risks are calculated using risk quotients (RQs). With these measures, the Agency can adequately consider 1) the magnitude of the risk, and 2) describe who or what (non-target organisms) bears that risk.

As discussed above, in response to potential risks of concern, the Agency considers mitigation measures to reduce or eliminate an identified potential risk of concern. While the Agency considers mitigation measures for a given pesticide, the risk managers are tasked with weighing

[77] Environmental Protection Agency. 2010. Guidelines for preparing economic analyses. Accessed online on October 26, 2023 at: https://www.epa.gov/environmental-economics/guidelines-preparing-economic-analyses.

the reduction in risk of an added mitigation measure (i.e., increased Personal Protective Equipment (PPE), respirators, etc.) against the reduction in benefits that may result from the cost imposed by the mitigation. When possible, OPP will present the impacts that mitigation measures may have in monetary or quantitative terms and will also describe the burden that additional mitigation may impose in qualitative terms. For example, the Agency may consider the use of an enclosed cab to mitigate inhalation risks to applicators; however, if the Agency also finds that enclosed cabs are not commonly employed in the relevant use site(s) where the enclosed cab requirement would apply, then it would likely be economically insurmountable (given the difficulty to retrofit a tractor to be an enclosed cab and the prohibitively large cost that the purchase of new equipment may impose). A grower may rather utilize an alternative or a mix of alternative pesticides in its place, which would generally come at an increased quantitative and qualitative cost, since it is assumed that growers typically apply pesticides that incur the least cost while providing the most effective form of control. The Agency's current approach balancing risks against benefits, allows risk managers to consider the nature and magnitude of the risk and the benefits from the use of the pesticide, and to work through various mitigation options to reduce risks, while taking into consideration the economic, social, and environmental costs and benefits of the use of the pesticide. This approach allows EPA to comply with its FIFRA mandate for ensuring that pesticides meet the standard for registration.

Estimating the monetary costs of any health impacts resulting from exposure to paraquat would require consideration of many factors, including estimating the number of people who may suffer harm or the likelihood of any one person to suffer harm, the nature of the effect, and the likely consequences in terms of any medical bills and/or lost work. However, current risk assessment data and methodologies generally do not provide a quantitative measure of the 'clinical' outcomes that toxicity studies measure and do not incorporate these factors. EPA's LOC is based on the dosage at which there are no observable adverse effects and also takes into account multiple safety factors. As such, OPP's assessments do not allow for a translation from risk estimates to the specific effect that might be expected when risk estimates are above LOCs or to the likelihood of occurrence. Providing the cost of an outcome without providing the probability of the outcome may not help OPP make or explain regulatory decisions. Moreover, assigning a value estimate for potential bad health or ecological outcomes is difficult and often controversial. OPP has a long history of evaluating the risks (costs) of the use of a pesticide in terms of the risk estimates (e.g., MOEs), the severity of effects observed in the toxicity studies, and factors that may exacerbate or ameliorate likely exposures. Incorporating highly uncertain monetary measures is not likely to lead to substantially different or more protective decisions.

EPA did consider the cost of additional PPE as part of the benefits assessments. Additionally, the Paraquat PID and ID included the following:

> "In addition to monetary costs of respirators, the use of a respirator can reduce productivity of workers, which could increase time required to apply paraquat and increase costs. ….. If an applicator was unable to make lower acreage applications with a PF10 respirator or an enclosed cab, they could use an alternative herbicide, which could increase treatment costs."

One of the reasons that requiring PPE can reduce worker productivity is the need for more frequent breaks due to heat risks. That is, heat risks and reduced productivity are two different expressions of the same cost – workers who use substantial PPE in intense heat will either need to take more frequent breaks or else face heat-related risks (such as injuries and missed work). The Agency does not expect these mitigations to frequently result in heat-related injuries; rather, the Agency expects that people will take breaks before reaching that point. Given that taking breaks reduces productivity, the costs of this mitigation may be borne by the employer (if paying workers by the hour) or by the employee (if getting paid by the task).

As described in Section V.A., EPA has determined that there is insufficient evidence to link exposure from the pesticidal use of US registered paraquat products to PD in humans. Even with some of the inhalation and dermal risks not being fully mitigated, EPA does not believe there is concern for PD because the data do not support a connection between paraquat use as a pesticide and PD. Where an outcome is not considered a possible risk or cost of using the pesticide, that outcome is not measured as a risk in a risk-benefit balancing exercise; therefore, EPA did not weigh potential risks or health-care costs associated with PD as part of registration review. Even if EPA had considered PD to be an expected risk from the use of paraquat, which it does not, FIFRA does not require EPA to weigh that "cost" as a monetized health-care cost; it simply requires EPA to determine whether the risks are unreasonable, taking into account the economic, social, and environmental costs and benefits of the use of the pesticide. EPA's current approach of weighing the potential downside (risk or cost) from use of the pesticide with the potential upside (benefit) from use of the pesticide meets that standard.

G. Consideration of Risk-Benefit Balancing Rationale

EPA disagrees that its risk-benefit determination was flawed and unsupported. The Agency has further described its methodologies utilized for paraquat in Section III. above and the conclusions and decision for paraquat are further detailed in the Section VI. above. As mandated by FIFRA, the Agency considered the 'costs' or 'risks' and 'benefits' of paraquat use before issuing its Interim Decision for Paraquat.

EPA acknowledges that potential risks remained after implementation of the mitigation measures identified in the Paraquat ID to include potential inhalation risk associated with aerial application of paraquat as a cotton harvest aid, dermal risk associated with certain post application harvest activities, and inhalation risk associated with certain groundboom applications of paraquat.

To determine whether paraquat could meet the FIFRA standard for registration, i.e., whether these risks were not unreasonable when taking into account the economic, social, and environmental costs and benefits of the use of paraquat, EPA carefully weighed these remaining risks against the benefits. Namely, those benefits include high benefits for use as a harvest aid such as timely desiccation of cotton crop close to harvest, and high benefits associated with use as an herbicide due to its unique mode of action which makes it an effective tool for resistance management and targeting particularly problematic target weeds that are resistant to other mode of actions for those uses. In addition, the Agency considered available information about harvesting practices and technology, available use and usage information at the time of the

Paraquat ID, the fact that paraquat handlers are required to be certified applicators and trained on the risks associated with paraquat use when making its risk-benefit decision.

As stated in the Paraquat ID and throughout this document, EPA concluded that these risks were outweighed by the benefits of the use of paraquat. However, based on EPA's consideration of its previous risk management decision, EPA is considering prohibiting raker and tramper harvesting activities and requiring an enclosed cab for all groundboom applications of paraquat. EPA welcomes comments relevant to the remaining potential risks, current harvesting technology and use practices, typical application rates, and benefits of paraquat for consideration of potential additional paraquat mitigation.

Appendix A. Supplemental Occupational Aerial Applicator Inhalation and Post-Application Dermal Exposure Assessment for Cotton Harvesting

Previously, in the HHRA, which was informed by the findings of the Occupational and Residential Exposure Risk Assessment (ORE),[78] the occupational aerial applicator and occupational post-application dermal exposure assessment for cotton harvesting was assessed considering the single maximum aerial broadcast application rate of 1 lb paraquat cation /acre (pounds of cation is equivalent to pounds active ingredient or AI discussed elsewhere in this document). Upon review of the paraquat labels, while 1 lb paraquat cation/acre is consistent with the preemergent cotton (herbicide) use, the single maximum application rate for paraquat use as a cotton harvest aid is 0.5 lb paraquat cation/acre. Since the higher application rate of 1 lb paraquat cation/acre is inconsistent with paraquat use as a cotton harvest aid, the information provided herein reflects the aerial applicator inhalation and occupational post-application dermal exposure and risk estimates for paraquat cotton harvesting activities to reflect the lower registered rate of 0.5 lb paraquat cation/acre.

Related to the occupational handler exposure scenarios, the only remaining aerial application scenario that resulted in a risk of concern following mitigation outlined in the ID was for aerial applications to cotton for harvest aid use. Although risk assessments that would adequately represent this scenario were provided in the ORE and Paraquat ID[79] , the estimates did not specify the "cotton, desiccation/harvest aid" scenario. To clarify, this exposure scenario assumes 1,200 acres treated by an aerial applicator in a 24-hour time period at the 0.5 lb paraquat cation/acre and this use results in an inhalation MOE of 71 (LOC = 100).

In regard to the post-application exposure scenarios that occur during cotton harvesting activities, workers are expected to contact residues on cotton bolls directly for which a dislodgeable boll residue (DBR) study, conducted in accordance with Guideline # 875.2100, could be used to refine occupational post-application dermal exposure and risk estimates for the crop. For paraquat, chemical-specific DBR data are not available; therefore, default assumptions are used in the post-application assessment for cotton harvesting activities and the supplemental assessment continues to rely on these default assumptions.

Table 1 presents the occupational post-application non-cancer dermal exposure and risk estimates for paraquat use on cotton considering the single maximum application rate for paraquat use as a cotton harvest aid (0.5 lb paraquat cation/acre) and Table 2 presents the previously reported occupational post-application non-cancer dermal exposure and risk estimates for paraquat on cotton considering the 1.0 lb paraquat cation/acre[80] application rate. Under the supplemental risk estimates (Table 1) the number of days after treatment (DAT) required for

[78] Britton, W. 2019. EPA, Paraquat Dichloride: Occupational and Residential Registration Review and Risk Assessment. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0126
[79] This is represented in the ORE and Paraquat ID by the "Field crop, high acreage: Peas, Dried-Type" line.
[80] Table 2 in this Appendix presents the occupational post-application non-cancer dermal exposure and risk estimates for paraquat on cotton as previously reported in the HHRA.

reentry where estimated risks are not of concern (MOE ≥ 100) for cotton harvesting activities following paraquat use as a harvest aid, range from 4 to 21 days.

Table 1: Occupational Post-Application Non-Cancer Exposure and Risk Estimates for Paraquat on Cotton at 0.5 lb ai/acre

Activities	DBR[1]	Transfer Coefficient (cm^2/hr)	Dermal Dose (mg/kg/day)[2] (DAT0)	MOE[3] (DAT0)	MOE[3] (DAT7)	DAT[4] (MOE ≥ LOC)
Harvesting, Mechanical, Module Builder Operator	2.0	900	0.09	67	140	DAT4 (100)
Harvesting, Mechanical, Picker Operator		2,400	0.24	25	52	DAT14 (110)
Harvesting, Mechanical, Raker		2,400	0.24	25	52	DAT14 (110)
Harvesting, Mechanical, Tramper		5,050	0.51	12	25	DAT21 (110)

1. DBR = Application Rate (lb ai/A) × F × (1-D)t × 4.54E8 µg/lb × 2.47E-8 acre/cm2; where F = 2 and D = 0.10 per day
2. Daily Dermal Dose = [DFR/DBR (µg/cm2) × Transfer Coefficient × 0.001 mg/µg × 8 hrs/day] ÷ BW (80 kg).
3. MOE = POD (6 mg/kg/day) ÷ Daily Dermal Dose.
4. DAT = Day after treatment/application for MOE to be greater than the LOC (100).

Table 2: Occupational Post-Application Non-Cancer Exposure and Risk Estimates for Paraquat on Cotton at 1.0 lb ai/acre

Activities	DBR[1]	Transfer Coefficient (cm^2/hr)	Dermal Dose (mg/kg/day)[2] (DAT0)	MOE[3] (DAT0)	MOE[3] (DAT7)	DAT (MOE ≥ LOC)
Harvesting, Mechanical, Module Builder Operator	2.0	900	0.18	33	70	DAT11 (110)
Harvesting, Mechanical, Picker Operator		2,400	0.48	13	26	DAT20 (100)
Harvesting, Mechanical, Raker		2,400	0.48	13	26	DAT20 (100)
Harvesting, Mechanical, Tramper		5,050	1.0	5.9	12	DAT27 (100)

1. DBR = Application Rate (lb ai/A) × F × (1-D)t × 4.54E8 µg/lb × 2.47E-8 acre/cm2; where F = 2 and D = 0.10 per day
2. Daily Dermal Dose = [DFR/DBR (µg/cm2) × Transfer Coefficient × 0.001 mg/µg × 8 hrs/day] ÷ BW (80 kg).
3. MOE = POD (6 mg/kg/day) ÷ Daily Dermal Dose.
4. DAT = Day after treatment/application for MOE to be greater than the LOC (100)

Appendix B. Worker Protection and Additional Drift Incident Information

A. Additional information on the Application Exclusion Zone under the Worker Protection Standard (WPS)

The Application Exclusion Zone (AEZ) is meant to supplement the "Do Not Contact" regulatory requirement. That provision, which is part of the Worker Protection Standard (WPS), requires handler employers and handlers to assure that "no pesticide is applied so as to contact, either directly or through drift, any worker or other person, other than an appropriately trained and equipped handler." 40 C.F.R. 170.210(a). The AEZ is defined as "the area surrounding the point(s) of pesticide discharge from the application equipment that must generally be free of all persons during pesticide applications" and extends 100 feet horizontally from the application equipment in all directions during application when the pesticide is applied aerially, as a spray using a spray quality of smaller than medium, as a fumigant, smoke, mist, or fog and during air blast application; and 25 feet horizontally when a pesticide is sprayed from a height of greater than 12 inches from the planting medium using a spray quality of medium or larger. *See* Pesticides; Agricultural Worker Protection Standard Revisions, Final Rule, 80 FR 67496, 67557 (2015) (contains definition of AEZ at 40 C.F.R. 170.305). When applications of WPS-labeled pesticide products are in progress on an agricultural establishment, agricultural employers must not allow or direct any worker or other person to enter or to remain in the treated area or the AEZ that is within the boundaries of the establishment until the application is complete. After the application is complete, the AEZ no longer exists, and the treated area is subject to the restricted entry interval (REI) specified on the pesticide product labeling and to the relevant WPS restrictions after applications. The requirement for the agricultural employer to keep persons out of the AEZ only applies within the boundaries of the establishment because the agricultural employer cannot be expected to control persons off the establishment. However, applicators are required to immediately suspend the application if workers or persons other than handlers involved in the application are in the AEZ, whether on the establishment or beyond the boundaries of the establishment. When implemented as intended, the AEZ supplements the WPS "Do Not Contact" provision and further reduces the risk of pesticide contact, either directly or through spray, to agricultural workers and bystanders. EPA requires spray drift management measures such as droplet size, release height, and wind speed restrictions to mitigate both direct and indirect exposures.

B. Additional information on the Agency's review of incidents

Adverse health effects from of exposure to a pesticide can provide important feedback to the Agency; however, given the nature of self-reports, it is not always possible to confirm causation and therefore incident reports do not replace the data relied upon in Agency risk assessments. When it comes to risk management, the Agency considers the incident reports as important supplements to the risk assessments and in certain instances as stand-alone reports that may require Agency action.[81]

[81] For example, the Agency required risk mitigation measures for paraquat in 2016 after reviewing incident data. The Agency was alerted to a high number of severe human health incidents associated with paraquat use, which led

The Agency accesses available incident information in four databases. The incident data for the Tier II report prepared for paraquat was collected systematically, but differently, across the four different databases used by the Agency with respect to such issues as coverage, certainty/confidence, fields/parameters reported, and usability.[82] Particularly, the four databases analyzed by the Agency have varying levels of validating how likely the reported exposure is causally related to the reported outcome.

C. Paraquat incidents classified as drift-related from 1998-2018 per Agency review

As mentioned, the Agency prepared a Tier II report on human incidents in support of paraquat registration review.[83] The Tier II Human incident report found that the majority of paraquat incidents involved occupational pesticide applicators or handlers who were made ill while applying or mixing/loading paraquat. Spills, splashes, and equipment malfunctions were leading causes of paraquat exposure and the vast majority of paraquat incidents involved exposure to a single individual . Paraquat incidents involving drift were negligible, particularly given the larger applicator/handler exposure trend of concern identified. No large paraquat drift events involving multiple individuals were reported. Further, there were very few cases overall related to drift, all of which were low in severity and resolved rapidly. This is also true in the Center for Disease Control/-National Institute for Occupational Safety and Health Morbidity and Mortality Weekly Report (CDC/NIOSH MMWR) report on paraquat and diquat incidents, found online at: https://www.sciencedirect.com/science/article/pii/S0013935116300032?via%3Dihub.

Neither EPA nor the authors of this CDC MMWR paper found drift to be a root cause leading to paraquat incidents.

This Tier II review of paraquat human incidents can be broken down further by each of the four databases reviewed:

The Office of Pesticide Program's Incident Data System (IDS) records incidents in one of two modules: Main IDS and Aggregate IDS. Main IDS contains incidents resulting in higher severity

to an EPA's evaluation of incident data. The evaluation then prompted an in-depth statistical analysis of paraquat incidents. The results of the analysis led the Agency to pursue risk mitigation measures ahead of the typical registration review process (i.e., PIDs and IDs). EPA determined that the number and severity of human health incidents caused by the accidental ingestion of paraquat could be reduced by requiring specialized training for all paraquat users, enhanced label warning statements, and closed transfer system requirements for all non-bulk paraquat products, and by prohibiting use of paraquat by anyone other than certified applicators (even those under the direct supervision of the certified applicator). These requirements were implemented in December 2020. To measure the effectiveness of these mitigation measures in preventing incidents of accidental ingestion, the Agency will conduct a new incident analysis for paraquat in 2025 and again in 2030. For more information on the 2016 mitigation decision please see the *Paraquat Dichloride Human Health Mitigation Decision* in the docket (EPA-HQ-2011-0855).

[82] Evans, E. and Recore, S., D466902, 25-SEPT-2018. Available at https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0122

[83] Evans, E. and Recore, S., D466902, 25-SEPT-2018. Available at https://www.regulations.gov/document/EPA-HQ-OPP-2011-0855-0122

outcomes and provides more detail regarding case specifics. Between January 1, 2012 and February 6, 2018, there were 63 cases reported to Main IDS involving paraquat. Of the 63 cases reported, 53 were reported for the single chemical paraquat that occurred within the United States. Of the 53 single paraquat incidents in the United States, four incidents were classified as major severity, 43 incidents were classified as moderate severity, one incident was classified as minor severity, and one incident had unknown severity. The most often reported cause of paraquat exposure to the IDS is during application of a product (18 incidents, 34% of the reported incidents). The second most often reported cause of exposure was handling of a product (10 incidents, 19% of the reported incidents) followed by contact with a product (6 incidents, 11% of the reported incidents). The fourth most common reported cause of exposure was bystander exposure (5 incidents, 9% of the reported incidents).

Over the same period of time (January 1, 2012 to February 6, 2018), 61 incidents were reported to Aggregate IDS involving paraquat. These incidents were classified as minor severity meaning that the person alleged or exhibited some symptoms, but they were minimally traumatic, the symptoms resolved rapidly and usually involved skin, eye, or respiratory irritation.

The Center for Disease Control's National Institute for Occupational Safety and Health (CDC/NIOSH) manages a pesticide surveillance program and database entitled the Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides. This database includes pesticide illness case reports from multiple states from 1998-2014. Cases of pesticide-related illnesses in the SENSOR-Pesticides database are ascertained from a variety of sources including: reports from local Poison Control Centers, state Department of Labor workers' compensation claims when reported by physicians, reports from state Departments of Agriculture, and physician reports to state Department of Health. The SENSOR coordinators primarily focus their follow-up case investigation efforts on occupational pesticide incidents, however, both occupational and non-occupational incidents are included. From 1998-2014, the most current set of available SENSOR-Pesticides data at the time of the paraquat ID, there were a total of 140 cases involving paraquat. The majority of paraquat cases were work-related exposures (81%). The majority of paraquat cases reported to SENSOR were low in severity (68%) and 32% of paraquat cases were moderate, high, or fatal in severity.

Apart from the occupational paraquat incidents, there were 27 bystander paraquat cases reported. Of these, seven cases involved exposure to paraquat drift. All seven bystander drift cases reported to SENSOR-Pesticides were low in severity.

The National Pesticide Information Center (NPIC) is a cooperative effort between Oregon State University and EPA, which is funded by EPA to serve as a source of objective, science-based pesticide information and respond to inquiries from the public and to incidents. From January 1, 2008 to December 31, 2017, nine human incidents involving paraquat were reported to NPIC. Of the nine reported incidents, two were reported as symptomatic and classified as possibly related to paraquat exposure and were further reviewed. One incident involved drift and the other incident involved an applicator exposure due to equipment malfunction. The drift incident is described below:

"In 2015 a caller (male, age 60) reported that pesticides were being applied across the street from his home, the wind was coming from the north and northwest, and the spray drifted across the street onto caller's property, including his sweet corn and tomato plants. Caller said the corn and tomato plants died. Within a day or two of the application he, his wife (age 49), and his daughter (age 19) developed severe coughing and chest irritation, all three of them went to their respective physicians for their symptoms, caller was given amoxycillin by his physician, and the symptoms lasted about two weeks. Caller said he and his family were not aware of any pesticide smell or taste when the drift happened, so he is unsure exactly how they may have been exposed, but they were all at the home, both inside and outside, on the application days."

The Pesticide Illness Surveillance Program (PISP) maintains a database of pesticide-related illnesses and injuries. Case reports are received from physicians and via workers' compensation records. In a PISP from 2010-2014 a total of 16 cases involving paraquat were reported. Two of the 16 incidents were attributed to drift and are described below.

"A worker at the fence of a vineyard felt mist on his face and noticed a metallic taste, which he attributed to an application about 40 feet away on the neighboring property. His coworker smelled the chemical but did not feel it and did not become ill." The medical description accompanying the case included, "bad taste in mouth, dry eyes, burning skin, shallow breathing and coughing. Due to a lab error, there was a delay in testing residue samples collected in the field. When samples were tested about a month later, only the treated area sample was positive."

"Three workers applied an herbicide to an almond orchard. Despite his respirator, one of the workers noticed a strong smell he believed to be the pesticide and began to feel ill. When he reported his illness about an hour later he was taken in for care." The medical description accompanying the case included, "headache, vomiting, sweating, and chills. He reported that the headache was so unbearable it was hard to speak. At the emergency department, an RN noted he was already feeling ill prior. No other worker became ill. The worker had not been fit tested for his respirator."

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 18, 2024

MEMORANDUM

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

SUBJECT: Appendix C: Supplemental Consideration of International Maximum Residue Limits on Benefits from Use of Paraquat

FROM: Brad Kells, Ph.D., Economist
Charmaine Hanson, Economist
Economic Analysis Branch
Biological and Economic Analysis Division (7503M)

THRU: T J Wyatt, Chief
Economic Analysis Branch
Biological and Economic Analysis Division (7503M)

TO: Marianne Walters, Team Leader
Kelly Sherman, Chief
Risk Management and Implementation Branch III
Pesticide Re-evaluation Division (7508M)

PEER REVIEW PANEL: May 24, 2023

SUMMARY

Foreign import restrictions on commodities treated with a pesticide can impact the benefits a grower might expect to receive from a pesticide; to the extent the restrictions impose a burden on the grower, this burden can be taken into account as a reduction in the benefit of the pesticide. As a general matter, EPA's assessment of benefits, including prices growers can receive for their treated commodities, already incorporates outside market forces, e.g., pre-existing restrictions on imports of treated commodities, and the same applies to paraquat. EPA's 2020 benefit assessments already account for the impact of pre-existing foreign MRLs on the benefits of paraquat. EPA analyses are based on revenues obtained by growers, and EPA observed no difference in price received for commodities treated with paraquat compared to other conventionally produced commodities that were not treated with paraquat.

Regarding Thailand's new import restriction on paraquat-treated commodities specifically, implemented via a maximum residue limit (MRL) of zero, EPA concludes that it does not result in any changes in the estimated benefits of the use of paraquat by U.S. producers of these commodities. For the Thai import restriction to reduce the benefits of using paraquat, it would have to either depress the price of commodities produced with the use of paraquat relative to the price of commodities produced without paraquat, or it would have to impose a fixed cost on growers who use paraquat.

The primary exports of U.S. farmers to Thailand are soybeans and wheat. There is no evidence available to indicate that growers producing paraquat-treated wheat and soybeans receive a price penalty for their crops. Thailand makes up a small portion of the total demand for U.S. soybeans and wheat, and the majority of U.S. soybeans and wheat are not treated with paraquat; therefore, Thai importers would easily be able to find sufficient commodity available to certify as untreated and purchase for use and consumption within Thailand. U.S. growers who use paraquat, meanwhile, can target their products to either domestic consumption or sales to the rest of the world; again, as the Thai ban only restricts sales of paraquat-treated commodities from a small portion of the world market, growers who use paraquat would not have difficulties finding purchasers for their commodities at the world price. While there may be costs to certifying that a commodity is untreated, based on a report provided by USDA's Foreign Agricultural Service, Thai purchasers, not U.S. growers, bear these costs.

INTRODUCTION

Paraquat is a restricted use herbicide that offers contact control, but no residual soil activity in many registered crop sites (e.g., cotton, soybeans, wheat). Paraquat also has a variety of niche uses such as sucker control (e.g., orchard crops), desiccant use as a crop harvest aid (e.g., grains, tomato), and as a cover crop burndown (e.g., cucurbits).

As part of the registration review process for paraquat, BEAD assessed the benefits of the use of paraquat in various use sites; the findings were presented in four documents available in the paraquat docket (Docket ID: EPA-HQ-OPP-2009-0755). Given paraquat's characteristics and

considering other available weed control measures, BEAD determined that use of paraquat has high benefits for numerous crops and crop groups including artichoke, cotton, peanuts, soybeans, bulb vegetables, cucurbits, alfalfa, orchards, and vineyards. BEAD also found that the benefits of paraquat were low for various crops and non-crop groups including grains (e.g. corn, winter wheat and sorghum), tomato, and pastureland. Due to limited information for some use sites, BEAD found that the benefits are uncertain for nursery production, rights of way, commercial/industrial buildings, and storage yards.

In 2021, the Environmental Protection Agency (EPA) published an Interim Decision (ID) for paraquat (Docket ID: EPA-HQ-OPP-2009-0755). EPA required risk mitigation measures to reduce the human health and ecological risks of the use of paraquat but did not cancel paraquat entirely. EPA noted in the decision that any remaining potential risks were outweighed by the benefits associated with the use of paraquat.

Several parties ("Petitioners") challenged the Paraquat ID in the U.S. Court of Appeals for the Ninth Circuit. See *California Rural Legal Assistance Foundation, et al. v. USEPA*, Case No. 21-71287 (9th Cir.) In September 2022, the Court granted the EPA's unopposed motion to hold the case in abeyance to allow the Agency to further consider substantive issues raised by the Petitioners in relation to the Paraquat ID. In its declaration supporting the motion, EPA stated its intention to publish documents summarizing EPA's further consideration of those issues by January 2024 for public comment and then after taking significant public comment into consideration, finalize a document (or multiple documents) regarding those issues by January 17, 2025, and present next steps at that time if additional mitigation was determined to be appropriate.

This document presents further background on EPA's preliminary consideration of an issue raised by Petitioners concerning the impact of international MRLs on growers applying paraquat to their crops in support of "EPA's Preliminary Supplemental Consideration of Certain Issues in Support of its Interim Registration Review Decision for Paraquat" to be published January 2024.

BEAD first provides background information on the Thai MRL change, on U.S. agricultural exports to Thailand, and on U.S. agricultural use of paraquat. Then, BEAD discusses the mechanisms by which external trade policy, such as foreign MRLs, can reduce the benefits of a pesticide. Finally, BEAD considers whether existing trade policy or the imposition of the Thai MRL is likely to have reduced the benefits of paraquat to U.S. growers.

BACKGROUND

History of the Thai MRLs for Paraquat

In April 2020, Thailand announced a zero-tolerance MRL for paraquat and chlorpyrifos on imported commodities. This ban was expected to go into effect in June 2020.

In May, 2020, the USDA Foreign Agricultural Service (FAS) wrote a report finding that "potential agricultural export losses [as a result of the proposed Thai zero MRLs for paraquat and chlorpyrifos] will be approximately $0.9-1.1 billion per annum" (Preechajarn, 2020). This is the

value of "relevant agricultural commodities and products" that Thailand imports from the U.S. In this calculation, the report assumes that "[t]he ban, through imposition of zero MRLs, will shut down any imports of agricultural commodities as raw materials originating from countries where paraquat and chlorpyrifos are still used for agricultural cultivation, such as the United States…" The vast majority of the $0.9-1.1 billion calculated potential export loss is the value of U.S. wheat and soybean exports to Thailand.[1]

The USDA FAS wrote a second report in November 2020, finding that "The [Thai] wheat and soybean industries… have been working with their suppliers to obtain non-detectable certificates that comply with the LOD [limit of detection] levels" (Prasertsri & Chanikornpradit, 2020).

U.S. Agricultural Exports to Thailand

According to the USDA FAS report, "Thailand relies, almost entirely, on the importation of wheat grains, soybeans, and soybean meal. The report also notes that US suppliers account "for about 40% of total Thai wheat and soybean imports" (Prasertsri & Chanikornpradit, 2020). While the U.S. accounts for a substantial portion of Thai imports, Thailand is only a small portion of the U.S. export market. According to USDA NASS (National Agricultural Statistics Service) (2022), in 2020 and 2021, only about 2% of U.S.-exported soybeans were exported to Thailand, and about 3% of U.S.-exported wheat was exported to Thailand. And exports are themselves only a portion of total U.S. production. According to USDA Economic Research Service (ERS) (2021), only about half of the soybeans grown in the U.S. each year are exported. The ERS February 2023 Wheat Outlook (Sowell and Swearingen, 2023) also anticipated that about half of wheat grown in the U.S. is exported.

U.S. Use of Paraquat in Soybean and Wheat

The majority of soybean and wheat acres grown in the United States are not treated with paraquat. From 2017 to 2021, only about 6% of soybeans and 2.5% of wheat (in percent crop treated) grown in the United States was treated with paraquat as an herbicide on average each year (Kynetec, 2022). Paraquat can also be used as a desiccant; this use pattern was not observed in soybean or wheat in USDA's National Agricultural Statistics Survey from 2017 to 2022 (USDA NASS, 2023a), but information submitted to BEAD by extension agents in Arkansas, Louisiana, and Mississippi indicates that 80-90% of the soybeans grown in these three states (about 3.5 million acres of soybeans) are treated with paraquat as a desiccant (Chism, 2021a, 2021b, 2021c). Based on best professional judgment, BEAD expects that soybean growers in other regions bordering the Mississippi Delta, including the bootheel of Missouri and Western Tennessee and Kentucky, also use paraquat as a desiccant. Desiccants are infrequently used in soybean production north of this area, as the shorter growing season and lower weed pressure in other soybean production regions reduces the need for chemical desiccation. If (as an upper bound estimate) 85% of all soybeans in the Mid-South (AR, KY, LA, MO, MS, TN) were treated with paraquat as a desiccant, this is equivalent to 15% of U.S. soybean acres[2]. Thus, BEAD

[1] At the time of writing, the USDA FAS was uncertain whether the Thai MRL would apply to feed ingredients, and so provided a range for potential losses.

[2] U.S. soybean production from 2017-2021 averaged 84.2 million acres harvested annually, of which 15.2 million acres are harvested in the Mid-South (USDA NASS, 2023a).

concludes that 6-21% of U.S. soybean acres are likely treated annually with paraquat as either an herbicide or a desiccant. Much of the usage of paraquat as an herbicide in soybeans is concentrated in the same region of the U.S. where paraquat is used as desiccant in soybeans (i.e., the Mid-South) (Kynetec, 2022), and so BEAD expects that many of the acres treated with paraquat as a desiccant are also treated with paraquat as an herbicide.

Maximum Residue Limits

The USDA FAS (Sirikeratikul, 2020) provides information on the requirements for importing agricultural commodities into Thailand. Importers can receive a Certificate of Analysis (COA) verifying that a commodity does not have residues of a pesticide (such as paraquat), issued by a testing lab that meets Thailand's accreditation standards; imports with a COA will not be detained on import to Thailand. Imports without a COA may be randomly sampled and tested by Thai authorities; if the shipment is randomly sampled and found to have pesticides residues above Thailand's MRLs, the shipment will be refused, and the importer will face increased testing on their imports in the future. Refused shipments are likely to be a substantial cost to importers. For example, these shipments may need to be destroyed, or storage fees may be incurred until the shipment can be sent elsewhere to be sold.

In order to be confident that their commodities can either receive a COA or else can pass random sampling, importers need to be able to assure that their commodities are not treated with pesticides in such a way that the commodity will exceed the MRL of an importing country. Importers do not always have a substantial amount of information about the production practices of commodity producers. Typically, growers who produce conventional commodity crops like soybean and wheat sell their produce to grain elevators, who combine crops from multiple growers into a single homogeneous product. It is not usually possible for a buyer who purchases soybeans or wheat from a grain elevator to be able to ascertain whether or not a particular pesticide was utilized in the production of a particular bushel of commodity: that bushel could contain some produce that was treated with a pesticide, as well as other produce that was not treated.

Organic production illustrates that it is possible for supply chains to keep produce separated based on its production practices and verify this separation to end purchasers. Growers who produce organic commodities frequently face much higher production costs per unit of output than growers producing crops conventionally. Organic pest management is more complicated than conventional pest management because organic growers have a more limited toolkit for pest control. However, some consumers are willing to pay a price premium for organically-produced agricultural commodities. Growers, and consumers, rely on third-party certification that organic production practices are followed and the organic commodity must be kept separate from conventional crops through the supply chain the entire way from the field to the final purchasing consumer. Organic and conventional produce are, essentially, different commodities.

Thai importers will have to establish a system to ensure imported commodities, including U.S.-grown soybean and wheat, do not have paraquat residues. This could be achieved through sampling (probably prior to shipment), by obtaining certification that paraquat was not used in the production of the commodities, or simply by purchasing soybeans from production regions

that do not use paraquat. Such a system may result in increased costs to import commodities but, as explained in the next section, is unlikely to result in a price premium for paraquat-free commodities relative to commodities treated with paraquat.

EFFECT OF EXTERNAL TRADE POLICY ON U.S. AGRICULTURE

The benefits of a pesticide are what a grower gains from the use of the pesticide relative to the next best alternative pest control tool. Common benefits of pesticides include reduced pest control and production costs and/or improved pest control, which results in increases in yield or in crop quality. That is, in the absence of a pesticide, a grower would employ alternative control measures, which may result in higher pest control costs, higher operational costs (such as managerial costs or purchasing new equipment), and/or worse pest control resulting in yield/quality loss.

The benefits of a pesticide decrease if the gains of a grower who uses the pesticide decrease (e.g., the pest develops resistance to the pesticide and the level of control is reduced), but the benefits of a pesticide also decrease if the gains of the grower increase with the use of other control measures (e.g., the cost of alternatives falls). In either case, growers gain less from the use of the pesticide – the gap between user outcomes with and without the pesticide shrinks (and may even become negative).

Grower Benefits of Paraquat = [Grower Returns with the Use of Paraquat] – [Grower Returns without the Use of Paraquat]

Grower returns is equal to revenue minus costs. Grower revenue is the price that growers receive per unit sold multiplied by the units of their commodity sold. Costs include both variable costs (costs that vary with production, such as fertilizer, seed, and pesticides) and fixed costs (costs that are fixed regardless of production, such as land rental). The remainder is what the grower receives in return for his/her labor and managerial effort.

Returns = Revenue – Costs = [Units_Sold*Price_per_Unit] – [Variable_Costs + Fixed_Costs]

Thus, an MRL imposed in a foreign market can impact the benefits of a restricted pesticide by resulting in lower revenues if a grower uses the restricted pesticide (either by being unable to sell their product or by receiving a lower price per unit[3]) or higher costs if the grower uses the restricted pesticide.

IMPACT OF THAI PARAQUAT MRL ON THE BENEFITS OF PARAQUAT TO U.S. GROWERS.

BEAD next considers whether the Thai MRL for paraquat is likely to cause growers who use paraquat in the production of their crops to receive a lower price for their product relative to not using paraquat (either by being unable to sell their product or by receiving a lower price per unit), or to face higher costs (such as overhead and marketing costs).

[3] Equivalently, growers who do not use paraquat may receive a price premium for producing untreated commodities.

Revenue Loss

An import ban in a foreign market can result in U.S. growers who previously sold their treated commodities to the foreign market being unable to sell their treated produce if they cannot find an alternative market. This could occur, for instance, if the foreign market imposing the import ban was the sole purchaser of a commodity. An inability to sell a crop treated with a pesticide would reduce the benefits of the use of the pesticide in that crop.

Growers do not usually sell directly to final buyers. Instead, growers usually sell to commodity traders, who then sell commodities to final purchasers. Growers can either contract with traders prior to the start of a season, agreeing on price and quality standards for when the crop is harvested, or growers can sell their commodities to traders at market price at the end of the season.

In the short term, a commodity seller – such as a grower without a contract – may lose the entire value of a treated shipment of a crop if the intended foreign market will not accept the treated produce and the grower cannot find another buyer. In the long term, the inability to find purchasers for treated produce will result in growers not using the pesticide, thus losing all attendant advantages of the pesticide (such as lower control cost or higher yield) but being able to sell their crop.

As discussed in the Background section, Preechajarn (2020) concluded that "potential agricultural export losses will be approximately $0.9-1.1 billion per annum". This estimate implicitly assumes that U.S. growers who cannot export treated crops to Thailand also cannot sell their commodities to other purchasers. It is true that some growers who use paraquat may not be able to sell treated commodities to the Thai market.[4] However, crops produced by growers who do not use paraquat can be certified as untreated, and can still be sold to Thailand, or anywhere else in the world. And growers who do use paraquat can still sell to the world market. Other major importers of U.S.-grown wheat and soybeans, including China and the European Union, do allow the importation of crops treated with some amount of paraquat (BCGlobal, 2023).

BEAD concludes that U.S. growers who treat their wheat and soybeans with paraquat did not lose their ability to sell their produce.

A foreign import ban can also result in a decrease in demand for U.S.-produced treated commodities. If the foreign market constitutes a large portion of total world demand for the U.S. produced treated commodity, an import ban imposed by that market can result in a decrease in demand for the treated commodity, and a reduction in price received by growers who produce the treated commodity (this could occur via traders offering growers a lower price for treated commodities compared to untreated commodities). This results in a reduction in the benefits of the pesticide. We can take as an example a U.S.-produced commodity that is always produced using a particular pesticide. If a country which constitutes the majority of the demand for that commodity restricts the import of commodities treated with that pesticide, then the total world

[4] Soybean and wheat treated with paraquat prior to crop emergence may be able to pass the Thai MRL, because paraquat is not systemic and preemergence use may not leave a residue.

demand for the commodity will drop substantially. U.S. growers may still be able to sell the product to other countries, but due to the substantial leftward shift of demand, the glut of commodity on the world market may drive the price which growers receive down. This would reduce the benefits of the pesticide (growers could make more money producing other crops without the use of the pesticide).

However, in practice, an import ban will not necessarily result in a substantial decrease in demand for the treated commodity or a substantial increase in demand for the untreated commodity. The country imposing the ban may not account for a substantial portion of demand for the commodity, and not all U.S. growers may use the pesticide. In this case, even though the Thai market demands "untreated soybeans" rather than "any soybeans", the world demand for soybeans has not changed, and other purchasers will still buy treated soybeans. Growers who produce treated commodities may be able to sell (via middlemen) to the rest of the world market, while growers who produce untreated commodities may be able to sell to the country imposing the import ban. In situations where there remains a robust market for treated commodities and the new supply of treated commodities will not substantially shift the supply curve, growers who use the pesticide will not see a meaningful reduction in price received for their commodity. This means that an import ban on treated crops will not necessarily reduce revenue for producers of treated commodities, and so the benefits of the pesticide, in terms of revenue per unit of produce, are not necessarily reduced by a foreign market's imposition of the import ban.

EPA's analysis of the available usage data of paraquat on soybean and wheat demonstrate that paraquat usage is very limited. As discussed in the Background section, the majority of soybean (79-94%) and wheat (97%) acreage grown in the United States are not treated with paraquat and would be eligible to receive non-detectable certificates to sell their untreated commodities to Thailand.

As discussed in the Background section, less than 2% of U.S. grown soybeans and wheat are exported to Thailand. Since the majority of U.S. soybeans and wheat are not treated with paraquat, and because Thailand makes up such a small portion of total demand for U.S. soybeans and wheat, BEAD expects that Thai importers would easily be able to find sufficient commodity available to certify as untreated and purchase for use and consumption within Thailand. Further, Thai importers can also buy from growers in other countries who produce soybeans and wheat for export, provided those foreign growers can certify that their crops are not treated with paraquat.

U.S. growers who use paraquat, meanwhile, can target their products to either domestic consumption or sales to the rest of the world; again, as the Thai ban only restricts sales of paraquat-treated commodities from a small portion of the world market, BEAD expects that growers who use paraquat did not have difficulties finding purchasers for their commodities at the world price. Grain elevators are able to manage separate supply chains for commodity crops, with separate price points for different commodities – for instance, high oleic soybeans can be sold for a premium to some elevators (USB, 2022), which keep the beans in separate supply channels for sale to purchasers seeking the high oleic content for vegetable oil production. The November 2020 update from USDA FAS (Prasertsri & Chanikornpradit, 2020), however, does not suggest that Thai importers were paying a premium for paraquat-free commodities, and

BEAD is unaware of other evidence of a separate supply chain for soybean and wheat that are not treated with paraquat.

BEAD concludes that the Thai zero MRL did not result in U.S. growers who use paraquat receiving a lower price for their commodity compared to if they did not use paraquat.

Marketing Costs

BEAD does not expect that growers who use paraquat face any cost increases as a result of the new Thai MRL. There may be a cost for separating untreated commodities from treated commodities, for allocating untreated commodities to Thai purchasers, and for certifying those commodities as untreated, but BEAD expects that Thai purchasers have to pay these costs: Thailand is a small market for U.S. soybeans and wheat, and so U.S. growers can choose to sell their produce to the rest of the world market at world market prices, so Thai importers who wish to purchase U.S. soybeans and wheat have to purchase U.S. produce at market prices and pay for separation and certification[5]. As noted above, the November 2020 update from USDA FAS (Prasertsri & Chanikornpradit, 2020) does not suggest that soybean or wheat prices differ between treated and untreated commodities – suggesting that U.S. growers are selling at world prices regardless of their use of paraquat.

BEAD acknowledges that U.S. growers may have faced costs in the short-term as the market adjusted to Thailand's new zero MRL. However, the second FAS report indicates that flour mills in Thailand built up their inventory buying from suppliers who could not issue non-detectable certificates before the effective date of the new zero MRL (Prasertsri & Chanikornpradit, 2020). BEAD concludes that even these short-term costs likely accrued mainly to Thai importers and consumers rather than U.S. growers, and that long-term U.S. growers who use paraquat do not face any increases in overhead costs as a result of the Thai zero MRL.

EXISTING MRLS

While the Thai MRL on paraquat was being put into place at the same time that EPA was re-registering paraquat, other countries also have MRLs for paraquat that are lower than those in the United States. Petitioners in the paraquat litigation note, for example, that "the European Union's MRL for paraquat on soybeans is 3% what it is in the U.S. (0.02 ppm compared to 0.7 ppm) and for wheat is 2% of the U.S. (0.02 ppm compared to 1.1 ppm)."

BEAD agrees that foreign MRLs on pesticides that are lower than the US MRLcan influence the benefits of the pesticide. For instance, traders who export to a country with a lower MRL may be unwilling to purchase commodities treated with the pesticide due to concerns about rejection, and so growers may choose to not use the pesticide in order to meet purchase standards.

However, BEAD's existing assessments of the benefits of paraquat account for foreign MRLs, such as those in the European Union, that were in place at the time BEAD's assessments were

[5] "Separation" may be as simple as purchasing soybeans from areas of the United States that do not frequently use paraquat in soybean production.

produced. EPA analyses are based on revenues obtained by growers, and EPA observed no difference in price received for commodities treated with paraquat compared to other conventionally produced commodities that were not treated with paraquat. BEAD assessed the benefits of the use of paraquat in 2020, and so grower behavior at that point in time implicitly accounts for domestic and foreign regulation around paraquat that was currently in place. Growers are not obligated to use a pesticide if the use of the pesticide is contrary to their own economic interests, and so BEAD can conclude that growers who were using paraquat in 2020 had decided that they preferred paraquat to available alternatives, even after accounting for regulatory restrictions around paraquat (such as foreign MRLs).

CONCLUSION

Given the relatively small portion of the U.S. soy and wheat export markets that Thailand represents and the option for Thai importers to obtain non-detect certificates, the Thai MRL for paraquat of zero ppm did not result in any changes in net operating revenue for U.S. growers because it did not result in growers who use paraquat being unable to sell their product, seeing reduced sales, receiving a lower price for their commodity, or facing any increase in overhead costs. While there may be costs to certifying that a commodity is untreated, BEAD expects that Thai purchasers bear these costs, not U.S. growers. BEAD's 2020 benefit assessments already account for the impact of pre-existing foreign MRLs on the benefits of paraquat.

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